AD_____

Award Number: W81XWH-09-1-0730

TITLE: The Neurobiological Basis and Potential Modification of Emotional Intelligence through Affective / Behavioral Training

PRINCIPAL INVESTIGATOR: William D. Killgore, Ph.D.

CONTRACTING ORGANIZATION: McLean Hospital
Belmont, MA 02478

REPORT DATE: April 2013

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE *(DD-MM-YYYY)*	2. REPORT TYPE	3. DATES COVERED *(From - To)*
April 2013	Annual	25 September 2012 - 24 March 2013

4. TITLE AND SUBTITLE
The Neurobiological Basis and Potential Modification of Emotional Intelligence through Affective / Behavioral Training

5a. CONTRACT NUMBER

5b. GRANT NUMBER
W81XWH-09-1-0730

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
William D. Killgore, Ph.D.
Lauren Demers, B.A.
E-Mail: killgore@mclean.harvard.edu

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
McLean Hospital
Belmont, MA 02478-1041

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

Emotional intelligence (EI) is the ability to accurately perceive, understand, and use emotional information toward adaptive functioning. The goal of the present investigation is to understand the neurobiological basis of one aspect of emotional skills, known as emotional intelligence (EI), and to develop a training program to enhance these capacities. During the first 3 years of this study, 70 participants completed fMRI and EI testing. Analyses revealed that the functioning of inhibitory brain regions seems to be related to facets of personality, daytime sleepiness, and gender. Additionally, higher EI is associated with greater acuity of responses within interoceptive sensitivity brain regions to biologically/socially relevant stimuli (e.g., facial expressions) presented subliminally. Furthermore, results suggest that trait and ability EI are unique constructs, with trait EI closely related to personality and ability EI more correlated with standard cognitive intelligence (CI). Based on the preliminary findings from the neuroimaging study, a modification to the SOW was made which increased the study by an additional year in order to develop an EI modification program. During this next phase of the study, we are developing an internet-based 6 module-training program for enhancing EI skills. Once the materials are completed, we will collect pilot data on 60 healthy participants (30 in active EI training; 30 receiving non-EI training as a placebo control). Participant enrollment for this phase of the study will begin once HRPO approval is granted.

15. SUBJECT TERMS
Emotional Intelligence (EI), functional Magnetic Resonance Imaging (fMRI)

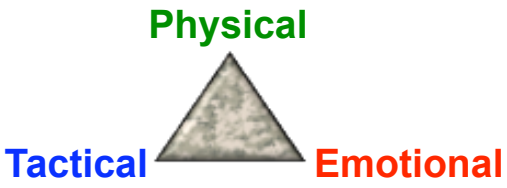
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRMC
U	U	U	UU	167	19b. TELEPHONE NUMBER *(include area code)*

Table of Contents

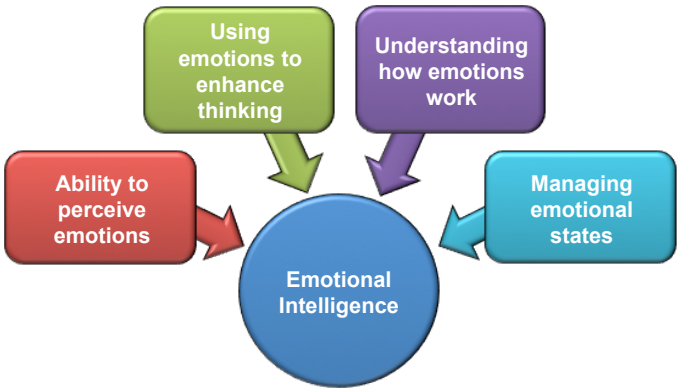
	Page
Introduction……..…..	**4**
Body……..	**5**
Key Research Accomplishments……..	**47**
Reportable Outcomes……	**47**
Conclusion……	**49**
References……	**50**
Appendices……	**51**

INTRODUCTION:

Military personnel are required to carry out difficult missions in demanding situations. The challenges of combat and peacekeeping missions require numerous skills, including physical capabilities and tactical skills. Additionally, the warfighter must be trained to deal effectively with the emotional stresses associated with military operations. Significant advances continue to be made in the development of new equipment, approaches to physical training, and education in tactical capabilities. However, comparatively little effort has been aimed at developing the emotional skills that Soldiers need to cope effectively with the stresses of combat or bounce back from the mental and emotional strains that are encountered during deployment. Just as a Soldier with inadequate training, poor physical conditioning, and insufficient body armor is at great risk of battlefield injury, so too a Soldier with poorly developed emotional capacities and fragile coping abilities is at increased risk for psychological wounds including depression, post-traumatic stress disorder, and even suicide. Renewed efforts to promote and develop emotional and mental resilience among warriors have led to the recent implementation of psychologically based initiatives such as the U.S. Army's Battlemind and Comprehensive Soldier Fitness programs. While these programs represent an important move to protect the mental health of Soldiers, they have been limited by the dearth of knowledge regarding the underlying neurobiology that contributes to the emotional capacities that allow a Soldier to cope effectively and remain resilient in the face of extreme and difficult challenges. More effective methods for developing these vital emotional skills are necessary.



The goal of the present investigation is to understand the neurobiological basis of one aspect of emotional skills, known as emotional intelligence (EI), and to develop a training program to enhance these capacities. EI can be defined as the ability to use emotions and emotional information to function adaptively across a variety of situations (1). There are a number of competing theories of EI, but one of the most widely accepted views suggests that EI comprises 4 major domains, including 1) the ability to perceive emotions in others, 2) the ability to use emotions to enhance thought processes and problem solving, 3) knowledge and understanding about how emotions work, and 4) the ability to manage and control emotional states to achieve long-term goal states. Just as standard cognitive intelligence provides the foundation for successful learning, problem solving, and adaptation to a variety of occupational, educational, and intellectual settings, it is likely that EI capacities provide the foundation for successful coping and resilience across a variety of emotionally challenging situations (2, 3), including those encountered during military operations. In order to effectively identify these capacities and promote their enhancement among Soldiers through targeted training programs, it will be necessary to



understand the brain-behavior links that serve as the foundation of EI. At present, there is almost no information regarding the underlying brain systems involved in EI (4). For the first 3 years of the project, this study has been aiming to fill this gap by collecting neuroimaging data during emotional tasks and correlating such data with trait and ability models of emotional intelligence. Near the completion of the initial project, we received notification that we were to receive an additional 1-year of supplemental funding to create and test a preliminary EI training program.

As part of our ongoing effort to develop a rapid EI training system, the initial study involved using functional neuroimaging to map the neurocircuitry associated with normal variations in EI traits and abilities. Over the 3-year funding period, 70 normal healthy participants ranging in age from 18 to 45 completed a comprehensive neurocognitive assessment battery that included two widely accepted measures of EI, assessment of standard cognitive intelligence (IQ), measures of coping, personality and resilience, as well as a host of emotional perception, decision-making, and problem solving tasks. These participants also underwent several structural and functional magnetic resonance imaging scans at 3 Tesla while engaged in a variety of affective probe tasks designed to engage specific aspects of the neurocircuitry hypothesized to contribute to EI. The major goals of the study include: 1) identification of the neurocircuitry that is parametrically related to variability in EI scores, 2) evaluation of how EI brain systems differ from those of standard cognitive intelligence, 3) determination of whether the two commercially available tests of EI are measuring similar or different hypothetical constructs, and 4) determination of which test of EI is most predictive of brain activation within the hypothesized neurocircuitry and actual performance on emotional tasks.

Data completion for the study was completed within the initial 3-year portion of the study and all accomplishments originally specified in the SOW have been completed. After completion of data collection during the first 3-years of the study, we requested a 6-month no-cost extension to allow continued analysis of the data for additional validation. The extension was granted and we now report interim findings since the last annual report. Near the end of the 6-month no-cost extension, we received an additional 1-year of supplemental funding to permit us to develop and pilot test a preliminary training program to enhancing EI capacities.

BODY:

1) All components of the initial SOW for the neuroimaging project have been accomplished.
2) We are moving forward toward accomplishing the goals of the modified SOW for the supplemental period that involves developing and testing a pilot training program for enhancing emotional intelligence. Thus far, the following goals have been accomplished:

a) A secure website server has been established for the program
b) 6 EI training (i.e., "internal awareness") modules have been researched and developed
c) 6 matched control (i.e., "external awareness) modules have been developed
d) All modules have been programmed into a prototype website program
e) Local IRB approval has been granted.

<u>Research Findings Pertaining to the Initial Neuroimaging Study</u>

We have continued to analyze the acquired data and report on these analyses. Over the course of the study, these analyses have yielded a total of 66 scientific abstracts and 15 peer reviewed publications being published. Abstracts and manuscripts since the third report are attached as an Appendix. Below is a summary of the new findings that have emerged since the third annual report:

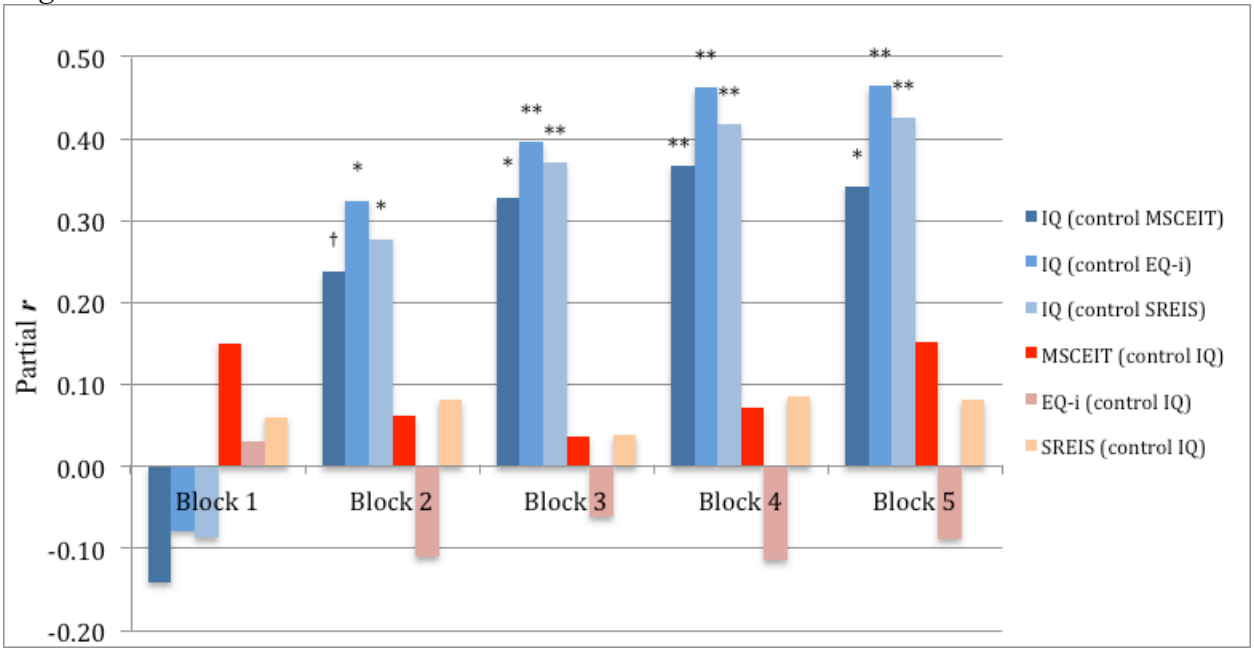
Validation of the Core Construct of Emotional Intelligence (EI)

We aimed to validate the basis of emotional intelligence (EI) as a construct and whether it is indeed unique from traditional IQ. We used ability and trait measures of EI, which themselves appear to evaluate different psychological constructs. Results indicated that significant variability in the self-report EI measures was accounted for by personality and emotional well-being measures, whereas the MSCEIT was more strongly associated with IQ. Overall, nearly two-thirds (62%) of the variance in EQ-i scores was accounted for by Big Five personality traits, emotional well-being and full scale IQ; whereas only 14% of the variance in MSCEIT scores was accounted for by these same variables. The present findings indicated that 1) competing measures of EI exhibit surprisingly small correlations with one another, and 2) significant variability in the self-report (but not performance-based) EI measures was accounted for by personality and emotional well-being measures. In summary, the current findings question the extent to which self-report measures of EI are appropriate given their substantial overlap with existing measures of personality and emotional state. This paper was recently published in the journal *Intelligence* (Webb, CA, Schwab, ZJ, Weber, M, DelDonno, SR, Kipman M, Weiner, MR, & **Killgore WD**. Convergent and divergent validity of integrative versus mixed model measures of emotional intelligence. Intelligence, 41, 149-156, 2013; see Appendix)

Cognitive versus Emotional Intelligence in Decision Making

Debate persists regarding the relative role of cognitive versus emotional processes in driving successful performance on the widely used Iowa Gambling Task (IGT). From the time of its initial development, patterns of IGT performance were commonly interpreted as primarily reflecting implicit, emotion-based processes. Surprisingly, little research has tried to directly compare the extent to which measures tapping relevant cognitive versus emotional competencies predict IGT performance in the same study. The current investigation attempts to address this question by comparing patterns of associations between IGT performance, cognitive intelligence (Wechsler Abbreviated Scale of Intelligence; WASI) and three commonly employed measures of emotional intelligence (EI; Mayer-Salovey-Caruso Emotional Intelligence Test, MSCEIT; Bar-On Emotion Quotient Inventory, EQ-i; Self-Rated Emotional Intelligence Scale, SREIS). Results indicated that IGT performance was more strongly associated with cognitive, than emotional, intelligence. As illustrated in the Figure below, after controlling for Full Scale IQ, there were no significant associations between any of the three EI measures and IGT performance across any blocks (for MSCEIT, all $r < .16$ & $p > .27$; for EQ-i, all $r < .04$ & $p > .41$; for SREIS, all $r < .09$ & $p > .53$). In contrast, when controlling for the different measures of EI, Full Scale IQ remained significantly associated with several IGT performance variables. Specifically, when controlling for MSCEIT scores, Full Scale IQ was significantly associated with IGT performance in blocks 3-5 (block 3, $r = .33$; $p = .016$; block 4, $r = .37$; $p = .006$; block 5, $r = .34$; $p = .011$). When controlling for EQ-i scores, Full Scale IQ was significantly associated with IGT

performance in blocks 2-5 (block 2, $r = .33$; $p = .016$; block 3, $r = .40$; $p = .003$; block 4, $r = .46$; $p < .001$; block 5, $r = .46$; $p < .001$). Similarly, when controlling for SREIS scores, Full Scale IQ was significantly associated with IGT performance in blocks 2-5 (block 2, $r = .28$; $p = .042$; block 3, $r = .37$; $p = .006$; block 4, $r = .42$; $p = .002$; block 5, $r = .43$; $p = .001$). To the extent that the IGT indeed mimics "real-world" decision-making, our findings, coupled with the results of other research discussed below, may highlight the role of deliberate, cognitive capacities over implicit, emotional processes in contributing to at least some domains of decision-making relevant to everyday life. This finding has been submitted for publication in the journal *Cognition*.

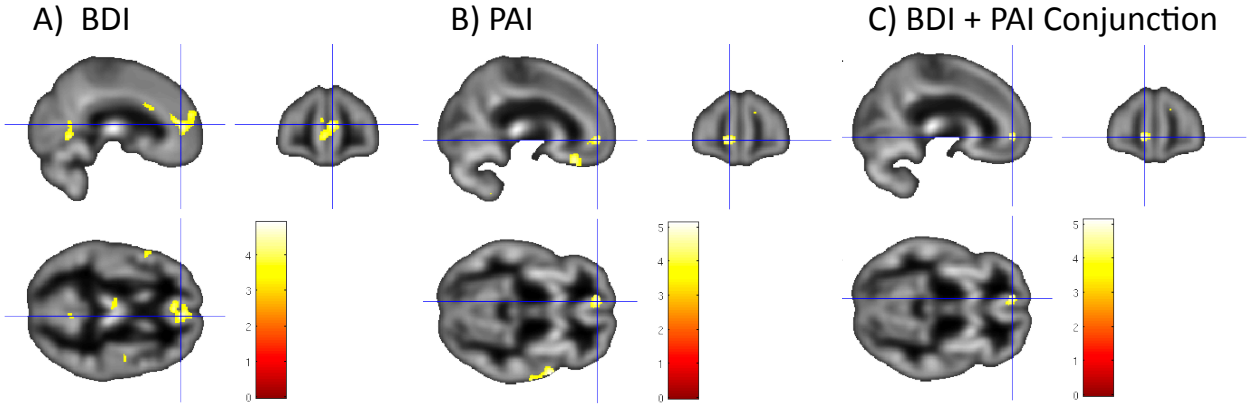


Gray Matter Volume and Mild Depression

Studies investigating structural brain abnormalities in depression have typically employed a categorical rather than dimensional approach to depression (i.e., comparing subjects with DSM-defined Major Depressive Disorder [MDD] vs. healthy controls). The National Institute of Mental Health (NIMH), through their Research Domain Criteria (RDoC) initiative, has encouraged a dimensional approach to the study of psychopathology as opposed to an overreliance on DSM-based diagnostic categories. Moreover, subthreshold levels of depressive symptoms (i.e., severity levels below DSM criteria) have been found to be associated with a range of negative outcomes, yet have been relatively neglected in neuroimaging research. To examine the extent to which depressive symptoms - even at subclinical levels - are linearly related to gray matter volume reductions in theoretically important brain regions, we employed whole-brain voxel-based morphometry (VBM) in a sample of 54 participants.

The severity of mild depressive symptoms, even in a subclinical population, was associated with reduced gray matter volume in the orbitofrontal cortex, anterior cingulate, and thalamus. A conjunction analysis revealed concordance across two separate measures of depression. Specifically, relatively higher BDI scores were associated with reduced gray matter volume in 16 clusters, including (i) bilateral anterior cingulate, bilateral medial frontal cortex and

left medial orbitofrontal cortex, (ii) bilateral anterior/mid cingulate, (iii) left thalamus and (iv) left insula (see Figure A below). Relatively higher PAI-Depression scores were associated with reduced gray matter volume in 9 clusters, including (i) left anterior cingulate and left medial orbitofrontal cortex (see Figure B below), (ii) bilateral medial orbitofrontal cortex and (iii) bilateral thalamus. The conjunction between the two primary analyses was used to identify the regions showing common overlap between the gray matter volume correlations for the two depression measures used in the current study. This analysis showed that the BDI and PAI-DEP scores were both associated with reduced gray matter volume in 4 common regions, including (i) left medial orbitofrontal cortex and anterior cingulate (see Figure C below), (ii) left thalamus, (iii) right superior medial frontal gyrus/superior frontal gyrus, and (iv) right superior temporal gyrus extending to the superior temporal pole.

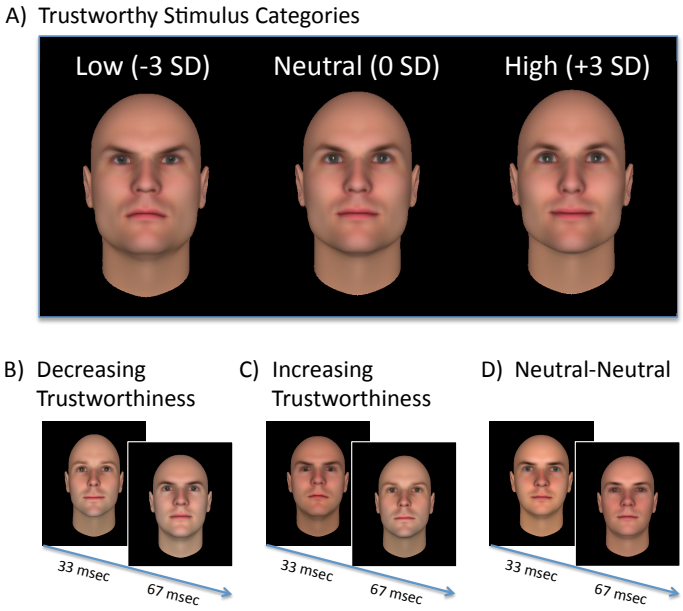


Reduced gray matter volume in theoretically important brain regions can be observed even in sample that does not meet DSM criteria for MDD, but who nevertheless report relatively elevated levels of depressive symptoms. Overall, and consistent with NIMH's RDoC initiative, these findings highlight the limitations of restricting the study of abnormal cognitive, emotional and behavioral processes in depression to DSM-based categorical comparisons, and the need for additional research using dimensional conceptual and analytic approaches.

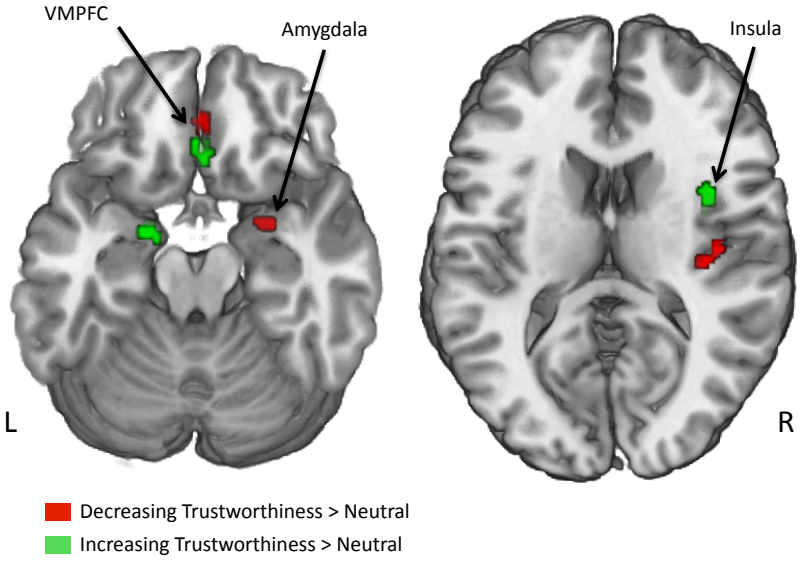
Emotional Intelligence and Dynamic Changes in Facial Trustworthiness

While little is known about the neurobiological substrates that underlie EI, some evidence suggests that these capacities may involve a core neurocircuitry involved in emotional decision-making that includes the ventromedial prefrontal cortex (vmPFC), anterior cingulate cortex (ACC), insula, and amygdala. In a sample of thirty-nine healthy volunteers (22 men; 17 women), scores on the Bar-On EQ-i (a Trait/Mixed model of EI) and Mayer-Salovey-Caruso Emotional Intelligence Test (MSCEIT; an Ability model of EI) were correlated with functional magnetic resonance imaging responses during brief presentations of moving facial expressions that changed in the level of perceived trustworthiness. As shown in *the figure below*, facial features were morphed along a continuum of trustworthiness according to the methods outlined by Oosterhof and Todorov (2008). A) Three categories of faces were used, selected from those rated 3 standard deviations (SD) below the mean in trustworthiness (left), those at the mean of trustworthiness (center), and those rated 3 SD above the mean in trustworthiness features (right). During the DFTT, pairs of faces were presented to give the appearance of subtle facial movement. B) During the *Decreasing Trustworthiness* presentations, a High Trustworthy face (+3 SD) was presented for 33 ms, followed by a Neutral Trustworthy face (0 SD) for 67 ms,

which gave the impression of movement toward lesser trustworthiness. C) During the *Increasing Trustworthiness* presentations, a Low Trustworthy face (-3 SD) was presented for 33 ms, followed by a Neutral Trustworthy face (0 SD) for 67 ms, which gave the impression of movement toward greater trustworthiness. D) During the *Neutral* presentations, a Neutral Trustworthy face (0 SD) was presented for 33 ms, followed by a different Neutral Trustworthy face (0 SD) for 67 ms, which provided a control for potential movement effects associated with changing face identities independent of changes in trustworthiness.



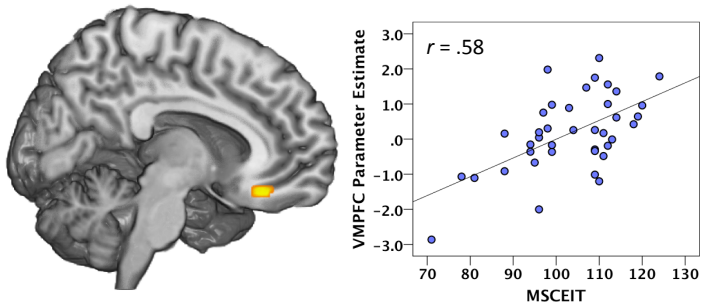
Core emotion neurocircuitry was responsive to dynamic changes in facial features, regardless of whether they reflected increases or decreases in apparent trustworthiness. In response to facial movements indicating decreasing trustworthiness, MSCEIT correlated positively with functional responses of the vmPFC and rostral ACC, whereas the EQ-i was unrelated to regional activation. The *Figure below* shows regions of functional activation associated with the contrasts between *Decreasing Trustworthiness* > *Neutral* (red) and *Increasing Trustworthiness* > *Neutral* (green). Significance was evaluated using a small volume correction for multiple comparisons within each search territory at $p < .001$ (uncorrected), $p < .10$, False Discovery Rate (FDR) corrected, k (extent) ≥ 10. The image shows that the *Decreasing Trustworthiness* > *Neutral* contrast was associated with increased activation of the ventromedial prefrontal cortex (vmPFC) and right amygdala (left image), and posterior insula (right image). The *Increasing Trustworthiness* > *Neutral* contrast was also associated with increased activation of the vmPFC as well as the left amygdala (left image) and anterior insula (right image).



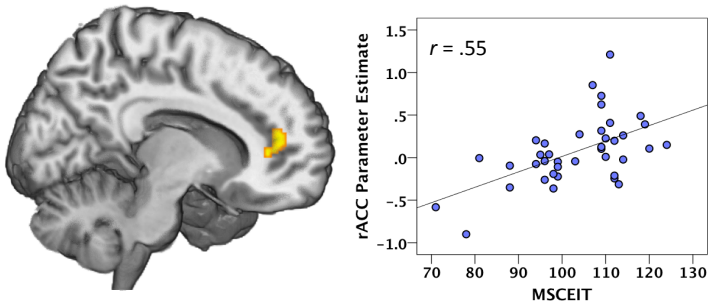
As evident below in the *Figure* below, there were significant clusters of activation that correlated with Emotional Intelligence (EI), $p < .10$ (small volume corrected), $k \geq 10$. A) Total scores on the MSCEIT were positively correlated with responses of the ventromedial prefrontal cortex (vmPFC) for the contrast of *Decreasing Trustworthiness* versus implicit baseline (left) [x = 6, y

= 32, z = -16]. For visualization purposes, the scatterplot (right) shows the relationship between MSCEIT scores and the first eigenvariate extracted for the entire correlated cluster. B) Total EI scores on the MSCEIT were positively correlated with responses within the rostral ACC (rACC) for the contrast of *Decreasing* versus *Increasing Trustworthiness* (left) [x = 14, y = 44, z = 12]. For visualization purposes, the scatterplot (right) shows the relationship between MSCEIT scores and the first eigenvariate extracted for the entire correlated cluster.

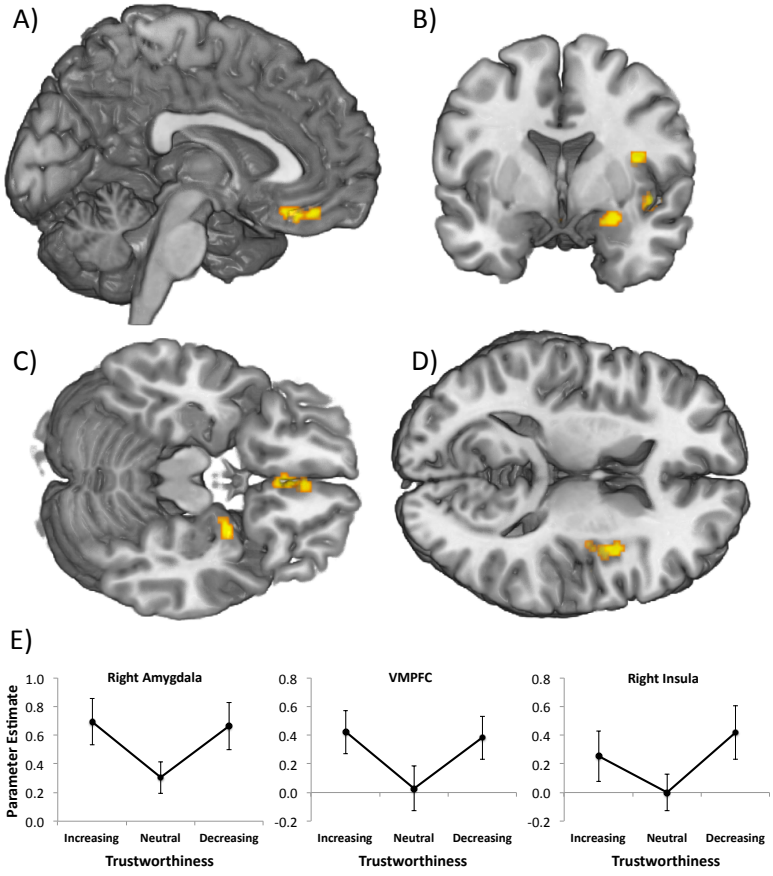
A) Decreasing Trustworthiness



B) Decreasing Trustworthiness > Increasing Trustworthiness



Finally, as shown in the *Figure* below, a trend analysis revealed a quadratic pattern of responsiveness across the 3 trustworthiness conditions of *Increasing Trustworthiness*, *Neutral*, and *Decreasing Trustworthiness* within key regions of interest, including the ventromedial prefrontal cortex (vmPFC), right amygdala, and right insula. Clusters showing this quadratic pattern can be seen on the A) sagittal slice (vmPFC), B) coronal slice (right amygdala and insula), and slices showing C) inferior axial (vmPFC and right amygdala), and D) superior axial (right insula) perspectives. E) Parameter estimates from the right amygdala, vmPFC, and right insula were extracted from the displayed clusters and plotted for visualization.



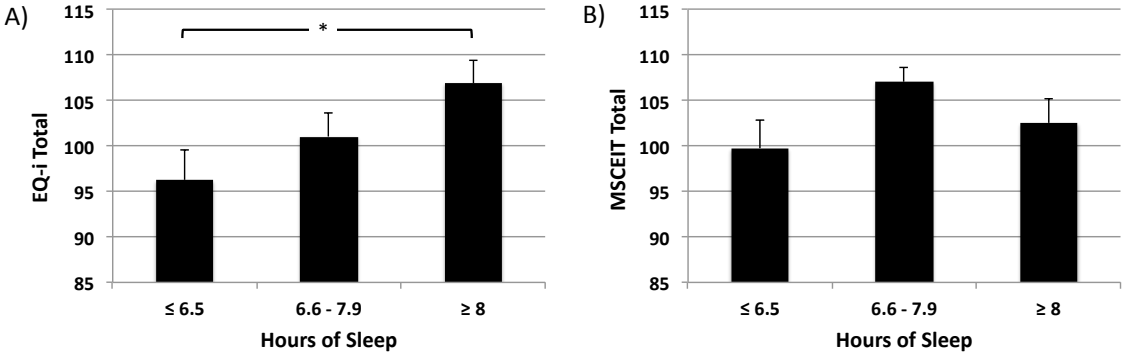
Overall, these findings suggest that greater EI was associated with increased responsiveness of the medial prefrontal cortex during a socially relevant dynamic face perception task, providing partial support for the role of the SMC in these capacities. Discrete nodes of the SMC, including the vmPFC and rostral ACC, were specifically correlated with *Ability* EI capacities, while *Trait* EI was not significantly related to the responsiveness of the hypothesized regions during dynamic facial displays communicating trustworthiness

information. Overall, systematic differences in EI capacities appear to be significantly related to the responsiveness of higher order emotion assessment and regulation regions of the medial prefrontal cortex and rostral anterior cingulate.

Sleep, Emotional Intelligence, and Cortico-Limbic Functional Connectivity

Prior research suggests that sleep deprivation is associated with declines in some aspects of emotional intelligence and increased severity on indices of psychological disturbance. Sleep deprivation is also associated with reduced prefrontal-amygdala functional connectivity, potentially reflecting impaired top-down modulation of emotion. It remains unknown whether this modified connectivity may be observed in relation to more typical levels of sleep curtailment. We examined whether self-reported sleep duration the night before an assessment would be associated with these effects. Participants documented their hours of sleep from the previous night, completed the Bar-On Emotional Quotient Inventory (EQ-i), Mayer-Salovey-Caruso Emotional Intelligence Test (MSCEIT), Personality Assessment Inventory (PAI), and underwent resting-state functional magnetic resonance imaging (fMRI). Sixty-five healthy adults (33 men, 32 women), ranging in age from 18-45 years underwent resting state functional connectivity scanning and completed measures of emotional intelligence and emotional functioning.

Greater self-reported sleep the preceding night was associated with higher scores on all scales of the EQ-i but not the MSCEIT, and with lower symptom severity scores on half of the psychopathology scales of the PAI. Longer sleep was also associated with stronger negative functional connectivity between the right ventromedial prefrontal cortex and amygdala. Moreover, greater negative connectivity between these regions was associated with higher EQ-i and lower symptom severity on the PAI. As shown in *Figure 5*, mean emotional intelligence



scores for the entire sample (n = 65) divided by terciles for Sleep Last Night, including Low Sleep (≤ 6.5 hours, n = 22), Moderate Sleep (6.6 – 7.9 hours, n = 21), and High Sleep (≥ 8 hours, n = 22). A) Analysis of variance indicated a significant main effect of sleep on scores on the Bar-On EQ-i (p = .032), with a significant difference between the High and Low Sleep groups. B) There was no main effect of sleep on the Mayer-Salovey-Caruso Emotional Intelligence Test (MSCEIT). *p < .05, corrected.

As evident in Figure 6, below, effect sizes of the correlations between hours of self-reported sleep obtained the preceding night and scores on the Bar-On Emotional Intelligence Inventory (EQ-i) and the Mayer-Salovey-Caruso Emotional Intelligence Test (MSCEIT). Black bars: All scales of the EQ-i showed significant Pearson correlations with *Sleep Last Night*, whereas none of the MSCEIT scales showed significant correlations. Gray bars: Similar trends were observed after statistically controlling for insomnia complaints, but only Adaptability remained significant. *$p < .05$, **$p < .005$.

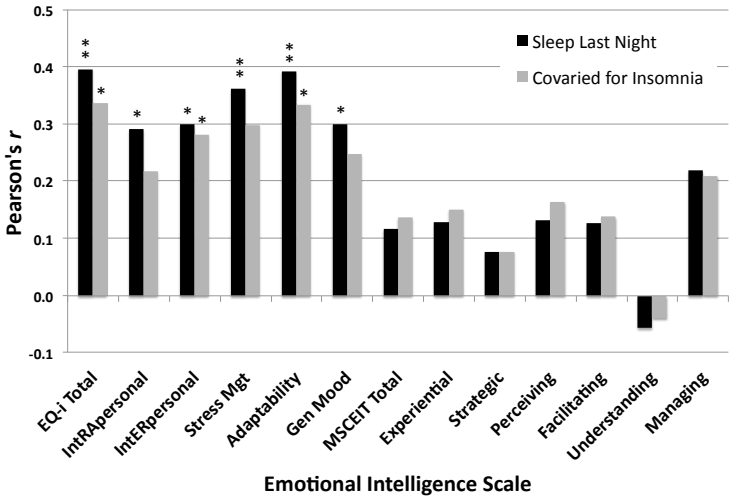
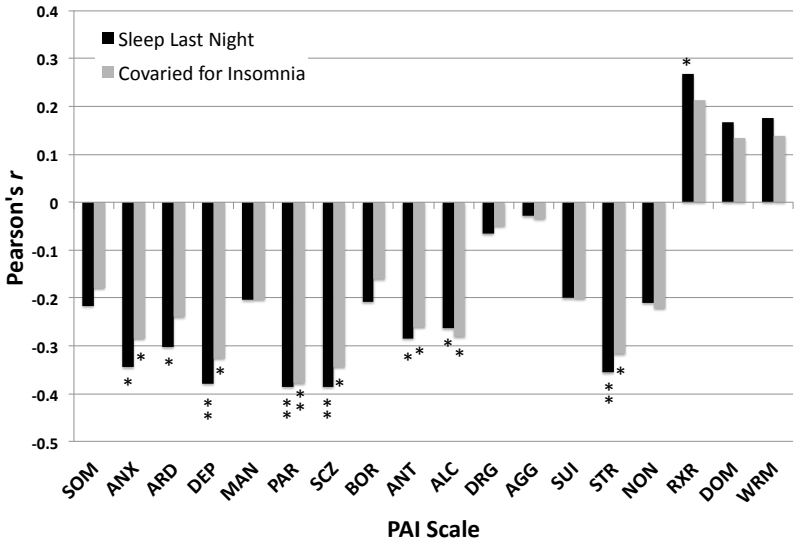


Figure 7 below shows the effect sizes of the correlations between hours of self-reported sleep obtained the preceding night and scores on the Personality Assessment Inventory (PAI). Black bars: Greater sleep the preceding night was associated with lower scores on several indices of psychopathology based on bivariate correlations. Gray Bars: Most of the correlations between *Sleep Last Night* and psychopathology remained significant after statistically controlling for insomnia complaints. *$p < .05$, **$p < .005$.



In *Figure 8*, the functional connectivity maps are displayed for the left and right vmPFC seed regions of interest (ROIs). The brain images show axial slices that include both the vmPFC and amygdala regions. The white arrows show the location of the amygdala target ROIs. The maps were set to a whole brain threshold of $p < .05$, FWE corrected for multiple comparisons.

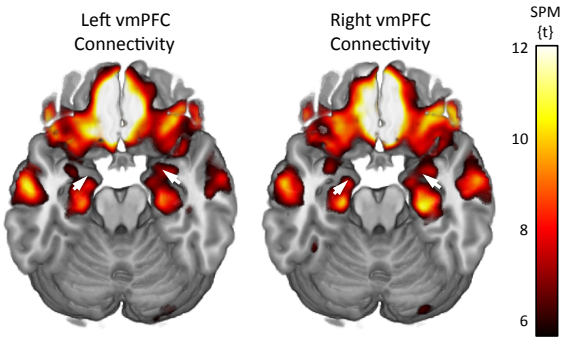
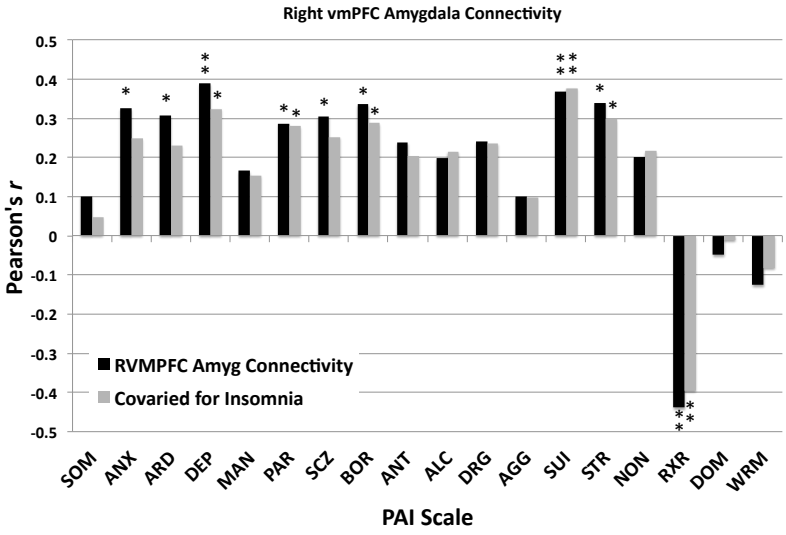
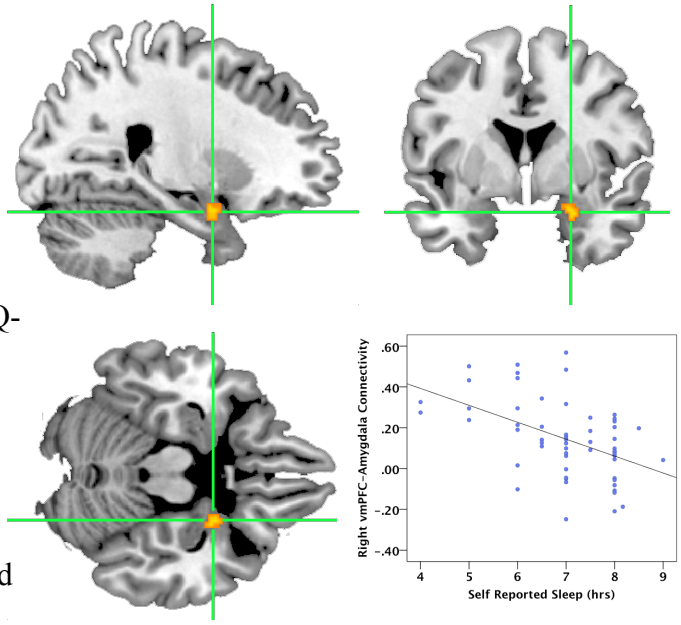


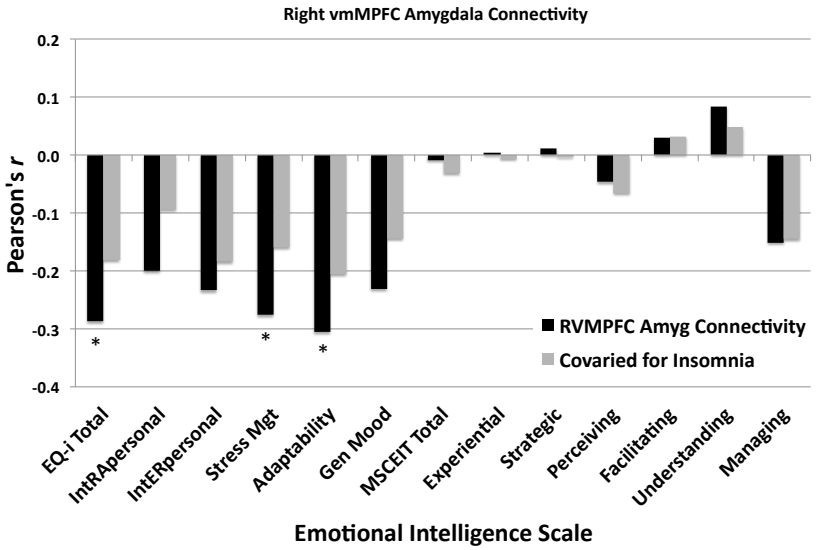
Figure 9 below shows that self-reported *Sleep Last Night* was significantly correlated with negative functional connectivity between the right

ventromedial prefrontal cortex (vmPFC) and the right amygdala. The figure shows the cluster in the right amygdala [MNI coordinates: x = 24, y = 2, z = -22] that showed negative functional connectivity with the right vmPFC seed region as a function of greater reported sleep time. For visualization, the cluster is height thresholded at ($p < .001$, uncorrected, spatial extent $p < .05$ FWE-corrected). Figures are displayed in sagittal (top left), axial (bottom left), and coronal (top right) views. The scatterplot (bottom right) shows the linear relationship between hours of sleep and the connectivity values extracted from the displayed cluster.





As evident in *Figure 10*, the effect sizes show the correlations between the magnitude of ventromedial prefrontal cortex (vmPFC) – amygdala functional connectivity and scores on the Bar-On Emotional Intelligence Inventory (EQ-i) and the Mayer-Salovey-Caruso Emotional Intelligence Test (MSCEIT). Black bars: Total EQ-i, as well as composite scale scores for Stress Management and Adaptability showed significant negative bivariate correlations with functional connectivity, indicating that higher emotional intelligence on the EQ-i was associated with greater *negative connectivity* between these two regions. In contrast, MSCEIT scales were not significantly correlated with functional connectivity between these two regions. Gray bars: After controlling for insomnia complaints, the observed correlations with emotional intelligence were no longer significant. *$p < .05$.

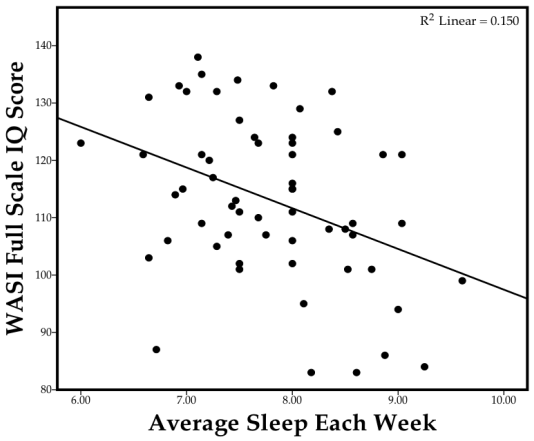


As evident in Figure 11, the effect sizes show the correlations between the magnitude of

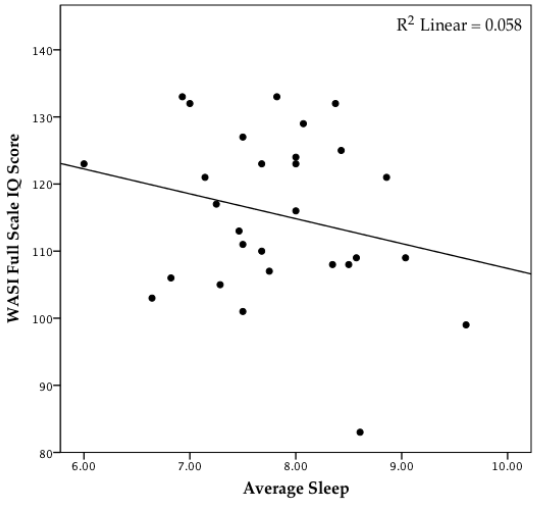
ventromedial prefrontal cortex (vmPFC) – amygdala functional connectivity and scores on the Personality Assessment Inventory (PAI). Black Bars: Scores on several PAI scales showed positive bivariate correlations with functional connectivity, indicating that symptoms of psychopathology tended to be higher as these two regions covaried positively together, while psychopathology was reduced as these two regions covaried negatively with one another. Gray bars: Partial correlations controlling for insomnia complaints remained significant for the majority of PAI scales. *$p < .05$, **$p < .005$.

Conclusions: Self-reported sleep duration from the preceding night was significantly correlated with negative prefrontal-amygdala connectivity, perceived emotional intelligence, and the severity of subjective psychological distress. More sleep was associated with higher emotional and psychological strength.

Sex Differences in the Association Between Sleep and Intelligence

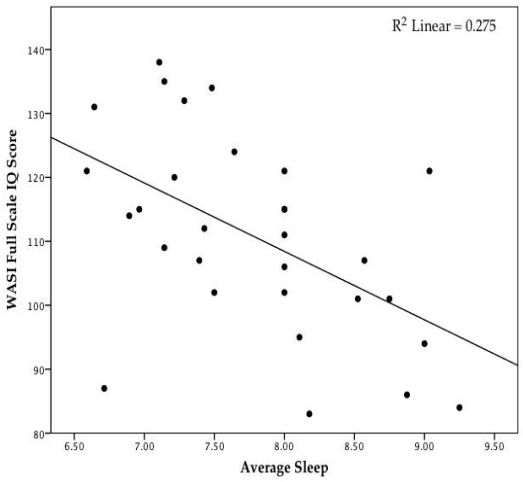


Another goal of the current research program has been to understand the role of sleep in various aspects of Cognitive and Emotional Intelligence. Sleep deprivation studies have demonstrated decreased performance on cognitive tasks with decreased sleep. However, the Neural Efficiency Hypothesis suggests that individuals of higher intelligence may possesses more efficient brain organization and thus require less sleep time for recovery of cognitive functioning. This perspective is also consistent with the Cognitive Reserve Hypothesis, which suggests that individuals with greater cognitive reserve are more efficient in using brain networks, and will tolerate more brain damage or strain (e.g., sleep deprivation) before experiencing functional impairment. In the present set of analyses, we examined relationships among IQ, gender, and sleep patterns in our sample of healthy adults.



Subjects completed a measure of standard intelligence (Wechsler Abbreviated Scale of Intelligence; WASI), the Epworth Sleepiness Scale (ESS), and a questionnaire about their sleep habits. Pearson correlations were used to explore the relationship between the Full Scale IQ of the WASI and the average number of hours of sleep on typical week- and weekend nights, controlling for age, education, ESS, and Socioeconomic Status (SES). To calculate SES, data was obtained on mean inflation-adjusted 12-month household income and the percentage below the poverty line of the participant's neighborhood based on home address (U.S. Census Bureau, 2010).

WASI Full Scale IQ scores were negatively correlated with the average amount of sleep (r=-0.437, p<0.01) (*Figure 1*). When analyzed by gender, no significant correlation was found between FSIQ and average nightly sleep in males (r= -.122). In females, a significant negative correlation was observed (r= -0.617, p<0.01) (*Figure 2*). A Fisher's z-transformation revealed that the two correlations differ significantly (z=2.01, p=0.04, two-tailed).



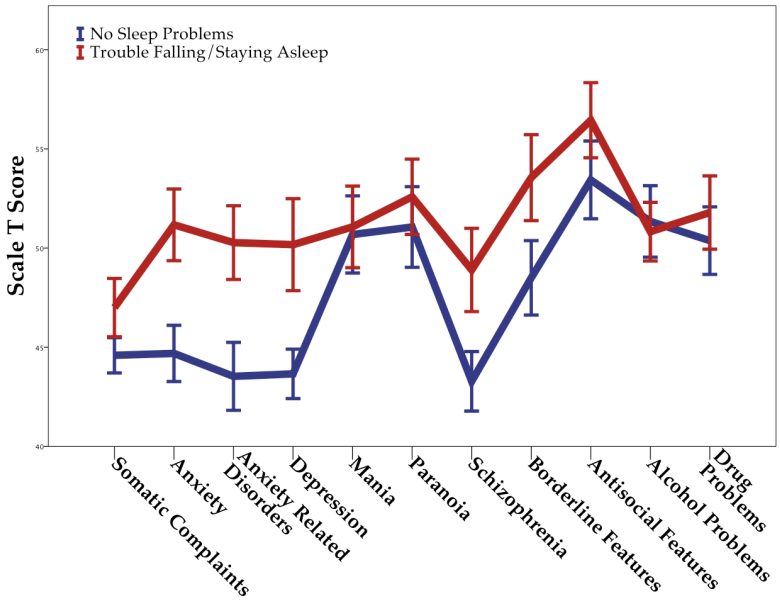
Findings suggest that females with greater intellectual ability obtain less sleep. Several possible explanations exist for this effect. The first supports the Neural Efficiency Hypothesis, indicating that individuals with higher cognitive functioning may also display higher efficiency in neuronal recovery during sleep. Another suggests that individuals with greater cognitive reserve may require less sleep to maintain the same level of functioning. Alternatively, individuals with shorter sleep duration may benefit from a longer period of wakefulness and greater opportunity for cognitive stimulation. Several key aspects may account for the gender disparity: previously identified differences in brain morpholo gy, particularly the role of white and gray matter in intellectual functioning; differences in levels of hormones, such as testosterone; and societal and cultural pressures specific to each gender, which may play into the differences in sleep habits and cognitive functioning.

Difficulty in Falling and Staying Asleep Linked to a Sub-Clinical Increase in Symptoms of Psychopathology.

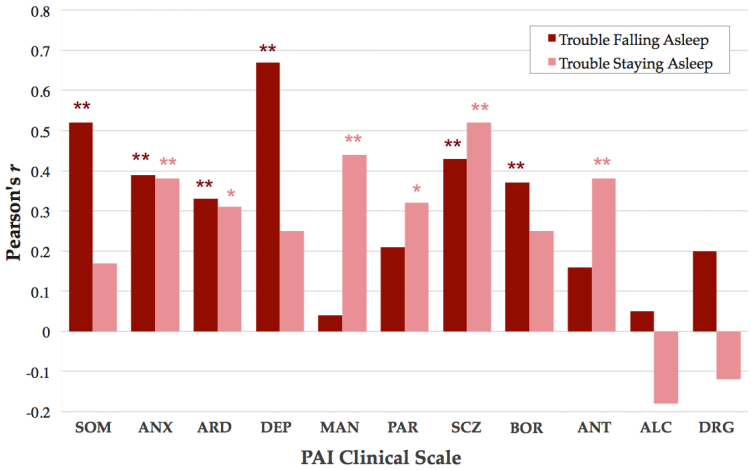
Sleep problems are linked with a broad spectrum of psychopathologies, particularly affective disorders. We have previously shown that laboratory sleep deprivation elicits significant increases in self-reported symptoms of psychopathology. Here we extend prior laboratory research to a non-laboratory naturalistic setting. We hypothesized that participants complaining of difficulties with sleep initiation or sleep maintenance would also score higher on measures of symptoms of psychopathology.

65 healthy adults completed a questionnaire on sleep habits and frequency experiencing trouble falling and/or staying asleep, along with the Personality Assessment Inventory (PAI) to assess clinical symptoms of psychopathology. A one-way MANOVA was used to assess differences in scores on PAI clinical scales between participants who had sleep difficulties and those that did not. Pearson correlations were used to evaluate the association between the frequency of estimated sleep disturbances per year and PAI scores.

Participants who endorsed sleep difficulties scored significantly higher ($p<0.05$) than those who did not on clinical scales measuring anxiety, anxiety-related disorders, depression, and schizophrenic symptoms. For these scales, further analysis of subscales was conducted using Bonferroni corrected one-way MANOVA. Subscale analyses revealed that scores on the Anxiety scale were elevated for Cognitive, Affective, and Physiological dimensions, while Anxiety-Related Disorders scores were driven predominantly by elevations in the Phobias subscale. Similarly, higher Depression scores among those with sleep complaints were driven predominantly by the Cognitive and Physiological subscales, while the elevated scores on the Schizophrenia scale were driven mostly by greater Psychotic Experiences scores. For individuals endorsing sleep onset problems, the reported frequency of these experiences was significantly correlated ($p < .05$, Bonferroni corrected) with increased Somatic Complaints, Anxiety, Depression, Schizophrenia, and Borderline Features. On the other hand, for individuals who reported having trouble staying asleep, the reported frequency of insomnia-related complaints was significantly correlated ($p < .05$, Bonferroni corrected) with higher measures of Anxiety, Mania, Schizophrenia, and Antisocial Features.



Difficulty with falling or staying asleep was associated with sub-clinical elevations in symptoms of psychopathology. Individuals reporting higher frequencies of sleep disturbances presented increased symptom severity across a number of clinical scales, suggesting a linear relationship between sleep disruption and psychopathological symptom complaints at a subclinical level. Furthermore, differences in associations were found between individuals who have trouble falling asleep and staying asleep. While causal directionality cannot be inferred, these findings support the notion that sleep plays a significant role in emotional functioning and may be an underlying risk factor for affective disorders.

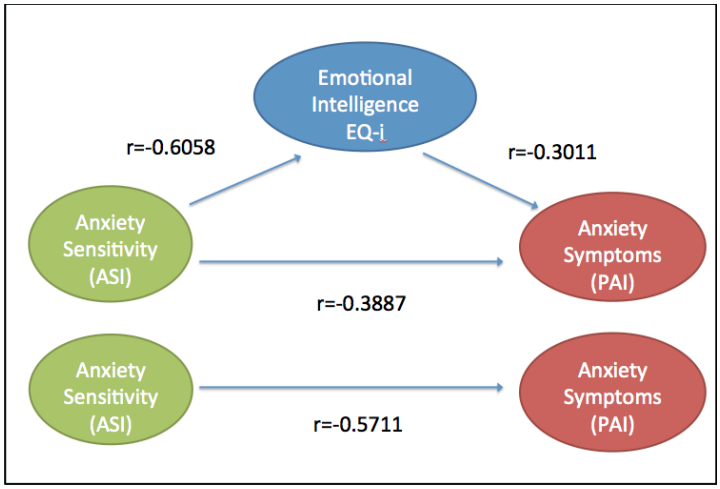


Emotional Intelligence as a Mediator of the Association between Anxiety Sensitivity and Anxiety Symptoms

The construct of Anxiety Sensitivity (AS), which refers to the fear of anxiety-related symptoms, including the physical sensations, thoughts, and social consequences associated with anxiety, has been theorized to be a cognitive vulnerability that contributes to the development of an anxiety disorder. However, the extent to which anxiety sensitivity predicts anxiety disorder symptoms may depend on emotional factors. Among individuals high in anxiety sensitivity, non-acceptance of emotional distress and less access to emotion regulation strategies is related to greater anxious arousal. We hypothesized that the level of Emotional Intelligence (EI) would mediate the relationship between AS and self-rated anxiety symptoms.

Sixty-one healthy adults (30 men) aged 18 to 45 completed measures of AS (Anxiety Sensitivity Index, ASI), anxiety symptoms (Personality Assessment Inventory, PAI), a "trait" measure of EI (Bar-On Emotional Quotient Inventory, EQ-i), and two "ability" measures of EI (Mayer-Salovey-Caruso Emotional Intelligence Test, MSCEIT; Self-Rated Emotional Intelligence Scale, SREIS). Mediation analyses were used to assess the influence of each of the measures of EI on the relationship between AS and anxiety symptoms.

EQ-i was a significant partial mediator of the relationship between AS and PAI anxiety symptoms ($z=2.95$, $p=.003$). However, there were no mediation effects for the ability measures of EI, either for MSCEIT scores ($z=.614$, $p=.539$) or SREIS ratings ($z=.549$, $p=.583$), on the relationship between AS and anxiety symptoms. Additional mediation analyses revealed that four of the subscales of the EQ-i (Intrapersonal, Stress Management, and General Mood) partially mediated the association between anxiety sensitivity and anxiety symptomatology, but there was no mediation effect for the Interpersonal subscale, $p=.3220$.



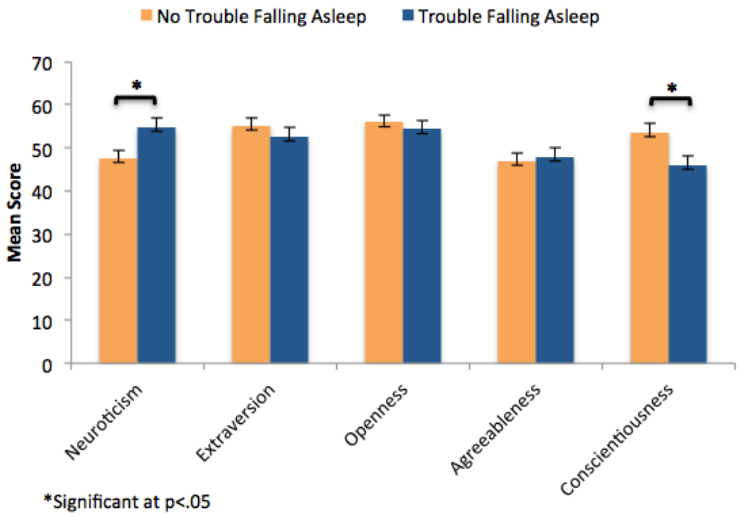
Findings showed that trait EI, but not ability EI, mediated the relationship between anxiety sensitivity and anxiety symptoms. Whereas the EQ-i measures a broad range of EI traits, which overlap with general emotional wellbeing, the MSCEIT and SREIS assess specific emotional skills. These findings suggest that factors related to emotional wellbeing, rather than specific emotional skills and abilities, mediate the relationship between anxiety sensitivity and anxiety symptoms. Findings may have implications for interventions designed to reduce anxiety by targeting the mediating factors.

Linking Sleep Initiation Trouble to Neuroticism, Emotional Control, and Impulsiveness

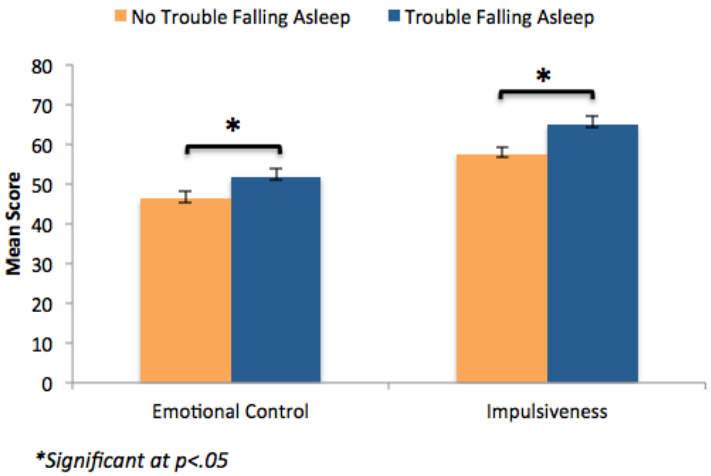
Difficulty initiating sleep is a key component of insomnia and a common symptom of many psychiatric disorders. Certain combinations of personality, cognitive and emotional factors may differentiate individuals with sleep onset problems from normal sleepers. For

example, neuroticism and impulsiveness are related to the subjective experience of insomnia and difficulty falling asleep. The cognitive model of insomnia argues that negatively toned cognitive activity triggers arousal and distress, which leads to a pattern of selective attention to sleep loss cues, erroneous beliefs about sleep loss, and maladaptive coping strategies that perpetuate sleep disturbance. Both neuroticism and impulsiveness may be accompanied by counterproductive methods to control negative thoughts and emotions that interfere with sleep. Neuroticism and cognitive and emotional arousal are vulnerability factors for insomnia. Furthermore, dysfunctional thought control strategies mediate the association between impulsiveness and insomnia. It was hypothesized that people who reported trouble falling asleep would have a higher degree of neuroticism, emotional control, and impulsiveness than normal sleepers and that minutes to fall asleep would be associated with these personality and cognitive factors.

Sixty-one healthy adults (31 men) aged 18 to 45 completed a questionnaire about typical sleep habits, indicating whether they had trouble falling asleep and how many minutes they took to fall asleep, the Revised NEO Personality Inventory (NEO-PI-R), the Courtauld Emotional Control Scale (CECS), and the Barratt Impulsiveness Scale (BIS). A multivariate analysis of variance was used to determine whether people who reported trouble falling asleep (N=26) differed from those who did not have trouble falling asleep (N=35) in terms of neuroticism, emotional control, and impulsiveness. Additionally, correlation analyses were used to examine relationships between minutes to fall asleep on weekdays and degree of neuroticism, emotional control, and impulsiveness.



People who reported trouble falling asleep differed from those who did not in terms of neuroticism, emotional control, and impulsiveness, (MANOVA, p=.015). Univariate between-groups comparisons revealed that trouble sleeping was associated with greater neuroticism (p=.013), emotional control (p=.042) and impulsiveness (p=.008). Minutes to fall asleep on weekdays was significantly positively associated with neuroticism (r=.475, p<.001) and impulsiveness (r=.394, p=.002),

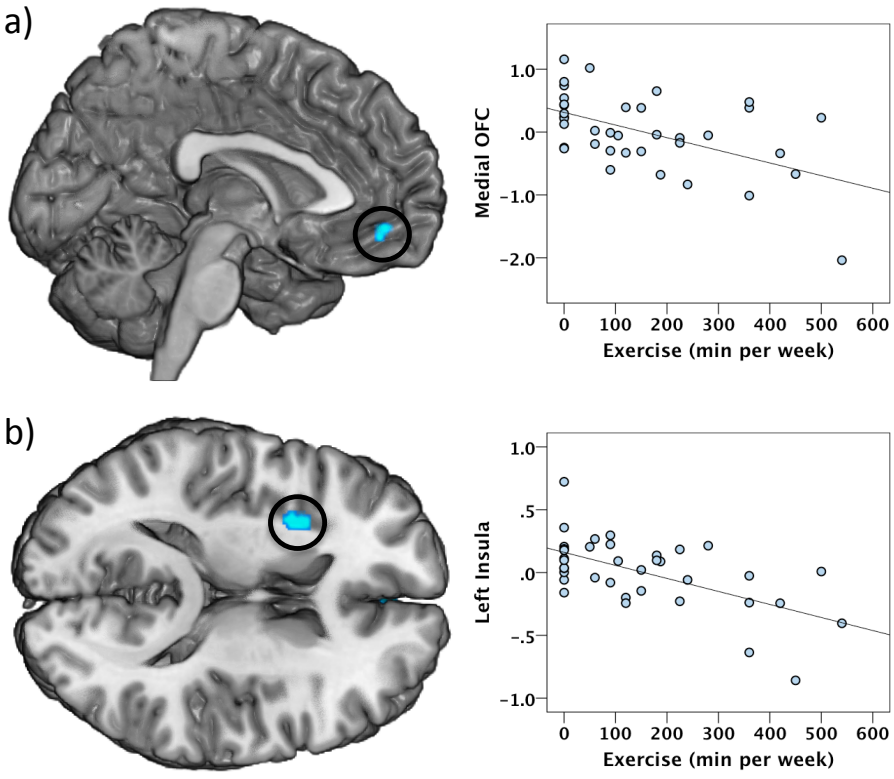


but not emotional control (p=.196).

Neuroticism, emotional control, and impulsiveness were higher in people with trouble falling asleep than normal sleepers. Likewise, minutes to fall asleep was associated with neuroticism and impulsiveness. These findings indicate that trouble falling asleep is related to degree of characteristic negative affect, the extent to which individuals are unable to cope with their negative emotions, and impulsiveness. Findings may have implications for treatment of sleep initiation trouble, mood disturbance, and impulsive behavior.

Physical Exercise and Brain Responses to Images of High Calorie Food

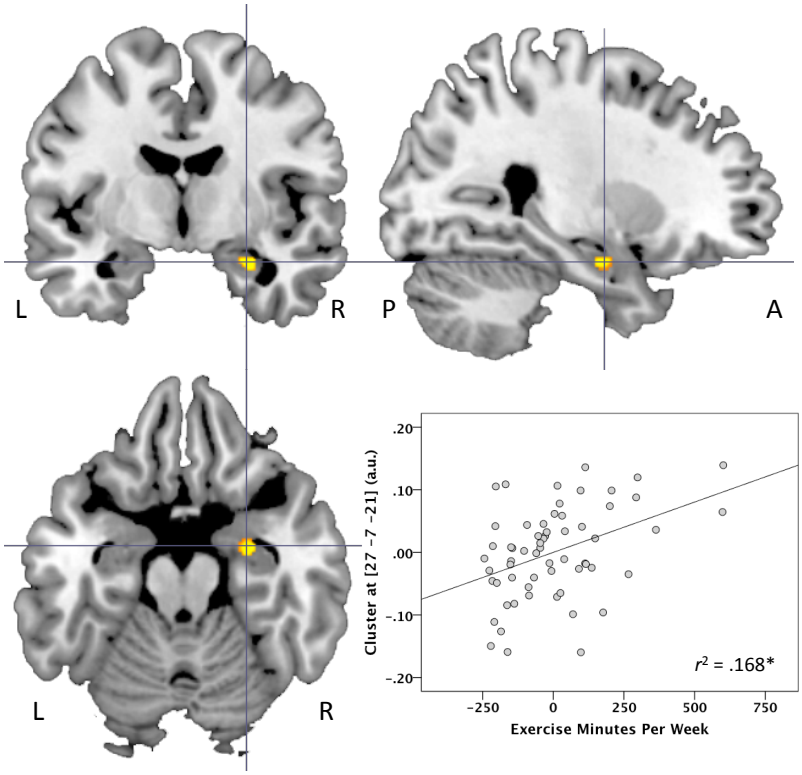
Physical exercise has many health benefits, including improved cardiovascular fitness, lean muscle development, increased metabolism, and weight loss, as well as positive effects on brain functioning and cognition. Recent evidence suggests that regular physical exercise may also affect the responsiveness of reward regions of the brain to food stimuli. We examined whether the total number of minutes of self-reported weekly physical exercise was related to the responsiveness of appetite and food reward related brain regions to visual presentations of high- and low-calorie food images during functional magnetic resonance imaging (fMRI). Secondly, we examined whether such responses would correlate with self-reported food preferences. While undergoing scanning, 37 healthy adults (22 men) viewed images of high- and low-calorie foods and provided desirability ratings for each food image. The correlation between exercise minutes per week and brain responses to the primary condition contrast (high-calorie > low-calorie) was evaluated within the amygdala, insula, and medial orbitofrontal cortex (mOFC), brain regions previously implicated in responses to food images. As evident in the figure, higher levels of exercise were significantly correlated with lower responsiveness within the mOFC and left insula to high-calorie foods. Furthermore, activation of these regions was positively correlated with preference ratings for high-calorie foods, particularly those with a savory flavor. These findings suggest that physical exercise may be associated with reduced activation in food-responsive reward regions, which are in turn associated with reduced preferences for unhealthy high-calorie foods. Physical exercise may confer secondary health benefits beyond its primary effects on cardiovascular fitness and



energy expenditure.

Physical Exercise and Brain Volume in Healthy Adults

Physical activity facilitates neurogenesis of dentate cells in the rodent hippocampus, a brain region critical for memory formation and spatial representation. Recent findings in humans also suggest that aerobic exercise can lead to increased hippocampal volume and enhanced cognitive functioning in children and elderly adults. However, the association between physical activity and hippocampal volume during the period from early adulthood through middle age has not been effectively explored. Here, we correlated the number of minutes of self-reported exercise per week with gray matter volume of the hippocampus using voxel-based morphometry (VBM) in 61 healthy adults ranging from 18 to 45 years of age. After controlling for age, gender, and intracranial volume, total minutes of weekly exercise correlated significantly with volume of the right hippocampus (see Figure). Findings highlight the importance of regular physical exercise to brain structure during early to middle adulthood.



<u>Research Findings Pertaining to the SOW Modification: Development of an EI Training Program</u>

Although not part of the initially funded study, a modification to the SOW was made during our no-cost extension after the third year of funding. This modification involved 1-year of additional funding to develop a pilot EI Training Program based on the Mayer-Salovey-Caruso Model of Emotional Intelligence.

According to the modified SOW, we will develop a 4-week internet-based training program to determine whether performance of specific EI tasks enhance EI capacities compared to a baseline measure. This will include comprehensive assessment of EI and affective skills pre- and post-training. The proposed project will involve two groups of healthy participants randomly assigned to either an EI Training group (TX; n = 30) or a placebo group (PLA; n = 30).

Both groups will complete 6 computer-based lessons over a 4-week period, with the specific content differing based on group assignment. Each lesson will be approximately 1 hour in length and will be presented via an online web-based server. We have experience with this type of system, as we are currently running a different study using a web-based treatment for depression. Based on our preliminary findings, the active TX lessons will be based on the Mayer-Salovey-Caruso 4-branch model of EI and will involve tasks designed to enhance the following aspects of emotional intelligence: 1) understanding emotions; 2) identifying emotions; 3) expressing and using emotions; 4) managing emotions.

The first of the six lessons will provide an overview of the 4-branch model of EI and guide the participant through some basic examples of each type of skill. Participants will then be given a homework assignment involving identification of relevant situations where EI principles might prove adaptive during the week. The second through fifth lesson will each focus on developing and enhancing a different branch ability of EI through programmed instruction and assessment tasks completed on-line. A brief homework assignment will also be required in order to generalize these skills to actual life situations and ensure that participants are actively engaged in the training. The final lesson will involve a review and integration of the previously acquired skill sets and a final homework assignment applying these skills in complex situations. The PLA group will also complete 6 online training sessions and homework assignments, but these will all involve an external environment awareness-training program, with no emphasis on specific emotional skills.

An important aspect of this validation objective will be the comprehensive assessment of change in EI from pre- to post-treatment. At the baseline and follow-up sessions, all participants will undergo a comprehensive assessment battery lasting approximately 5 hours. This battery will include the previously validated EI measures, including the Mayer-Salovey-Caruso Emotional Intelligence Test (MSCEIT), the Emotional Quotient Inventory (Bar-On EQi), the Self-Rated Emotional Intelligence Test (SREIT), Toronto Alexithymia Scale (TAS-20), Trait Meta-Mood Scale (TMMS), Emotion Regulation Questionnaire, Empathy Quotient, and Mindful Attention Awareness Scale, as well as a measure of cognitive intelligence (Wechsler Abbreviated Scale of Intelligence; WASI). Additional assessments will include resilience (Connor-Davidson Resilience Scale; CD-RISC), Personality (NEO-PI-R), and psychopathology (Personality Assessment Inventory; PAI). Computerized tests of emotional perception and decision-making will include the Reading the Mind through the Eyes Task, the Intuition Task, and Iowa Gambling Task (IGT).

The validation hypothesis is that individuals in the active TX group will show greater improvement in EI abilities, and that these changes will correlate with improvement on measures of resilience, emotional perception, emotional decision-making, and emotional control capacities.

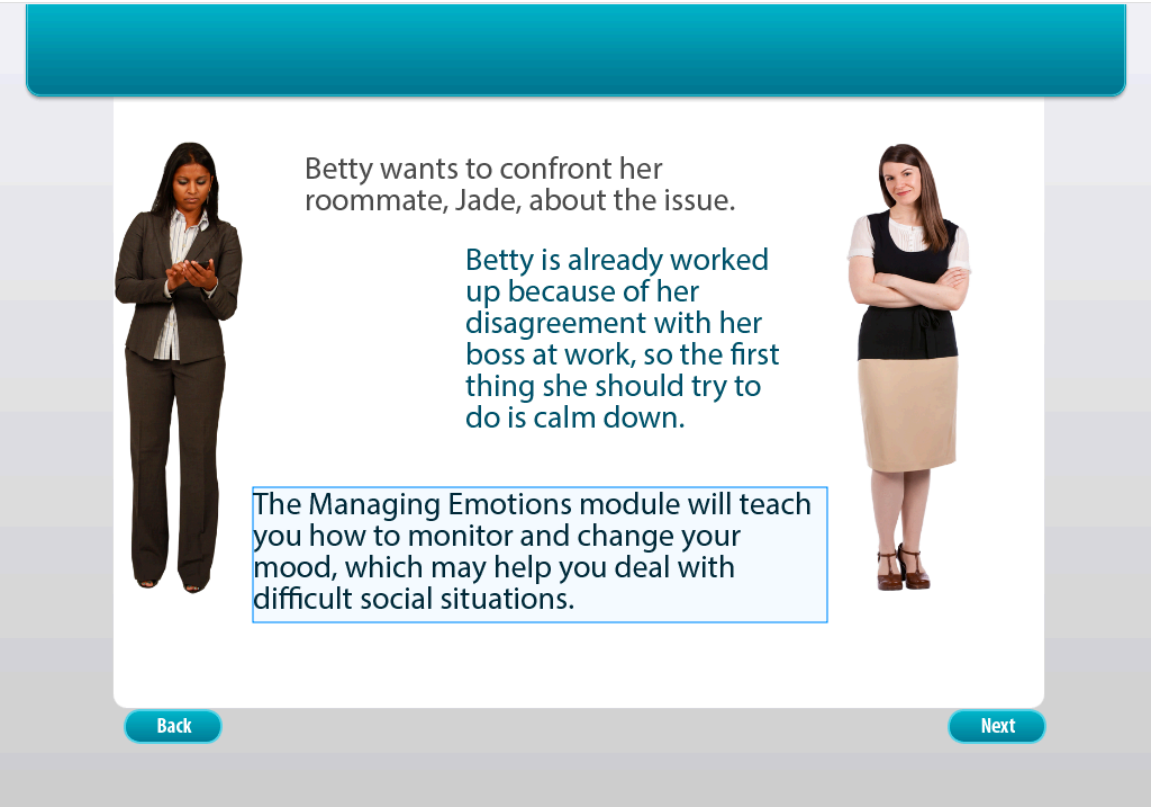
At present, we have now completed development of the training materials for the EI program and a matched non-EI control training program. The active treatment program, termed “Internal Awareness” and the control program, termed “External Awareness” are matched closely with regard to format, difficulty level, and time investment. The active Internal Awareness program includes 6 modules, including an introductory lesson, four lessons focusing on the four branches

of EI from the Mayer-Salovey-Caruso model of EI, and a final summary lesson. The control program is similar in format, but instead of focusing on internal feelings and emotions, the program teaches individuals to pay attention and understand their external environment (e.g., weather patterns).

The programs each last between 15 to 45 minutes to complete, depending on individual variability in participant engagement and reading speed. After each lesson, participants also complete a homework assignment. The next several pages provide a summary of the course content for the active EI (Internal Awareness) Training program, with example screen images of the program interface:

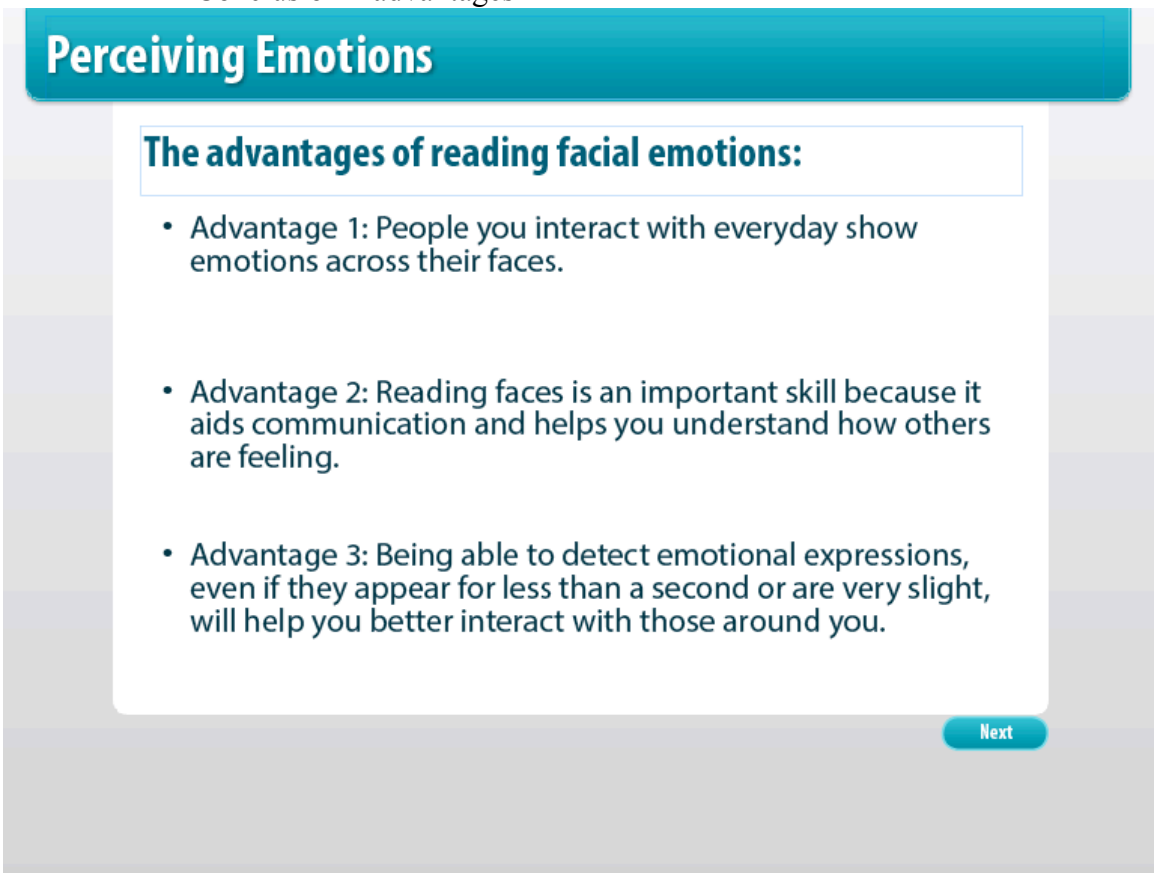
<u>Internal Awareness</u>

1) Introduction
   - Introduce program structure
   - Rationale for increasing internal awareness
   - Evolutionary perspective of value of emotions
   - Examples of how internal awareness is useful (with characters and scenarios)
   - True/False questions about common myths about emotional functioning
   - Introduce program content
   - Example of how program will be useful (with characters and scenarios)
   - Multiple choice questions about emotions most likely to be experienced in a situation
   - Conclusion



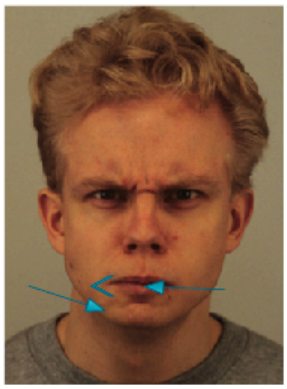
2) Perceiving Emotions

- Advantages of reading facial emotions
- Go through features of faces expressing the six basic emotions – focus on eyes and mouth. Use arrows pointing to each component.
    - Ekman descriptions of features/cues
    - Karolinska Directed Emotional Faces as stimuli
- Matching game: emotion to face
- Videos of people going from neutral to emotional expression -- first at normal speed and then slowed down with features previously taught described in real time (words show up at bottom of video as the person is expressing emotion)
    - The Amsterdam Dynamic Facial Expression Set videos
- Matching game: emotion to face
- 6 multiple choice: quick flashes of emotion (slow version – 3sec – and correct answer is displayed and explained)
- 48 multiple choice: quick flashes of emotion (fast version – 0.5sec – just correct answer is displayed, not explained)
- Conclusion – advantages



Anger: Mouth

- Jaw thrust forward
- Lips pressed together
- Lips narrowed
- Lower lip being pushed up



Next: Next
Surprise: Eyes

Click the response that corresponds with the correct emotion

- A) Anger
- B) Fear
- C) Sadness
- D) Disgust
- E) Happiness
- F) Surprise

Back

Submit

Good Job!

Now you can use your new skills to read emotional expressions on faces in your day-to-day life!

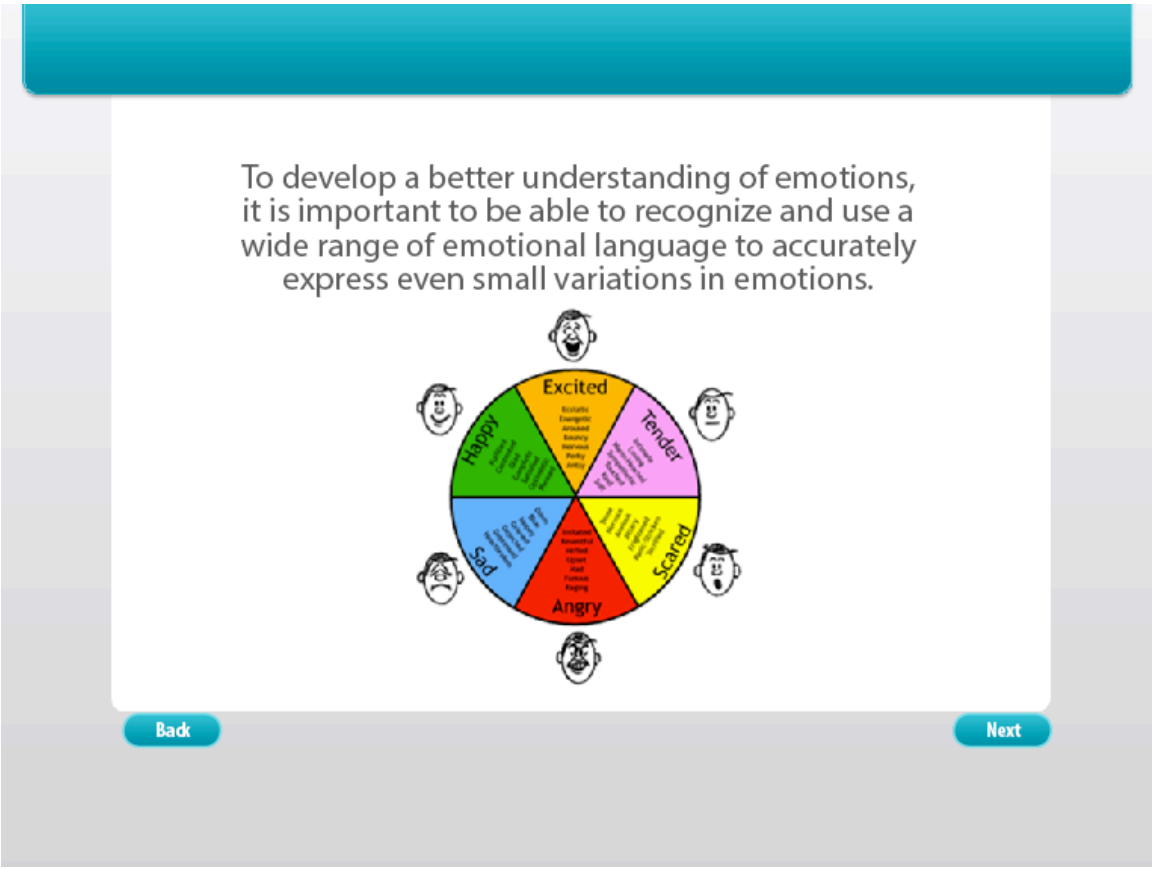
For instance, if someone is acting strangely and you are not sure why, perhaps trying to read his emotions shown on his face may help you understand what is going on.

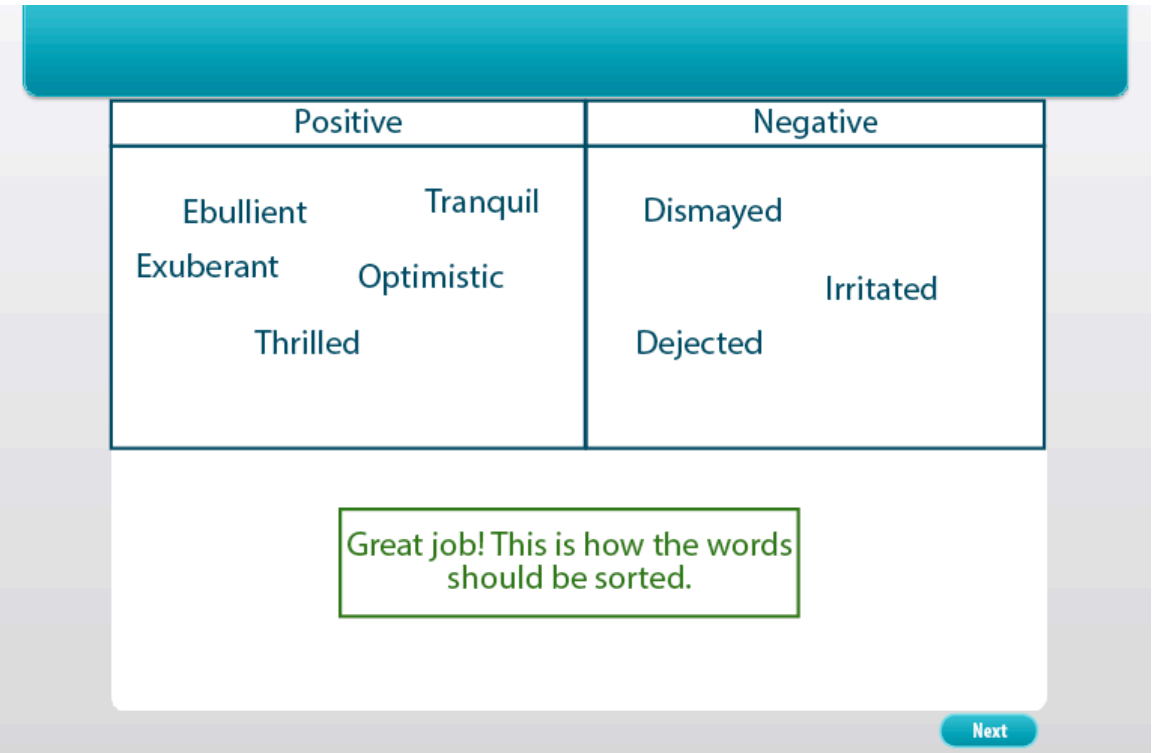
If you are having a discussion with someone and she is saying unexpected things, if you are able to read her emotions by looking at their facial features, you may be able to tell why she is acting this way.

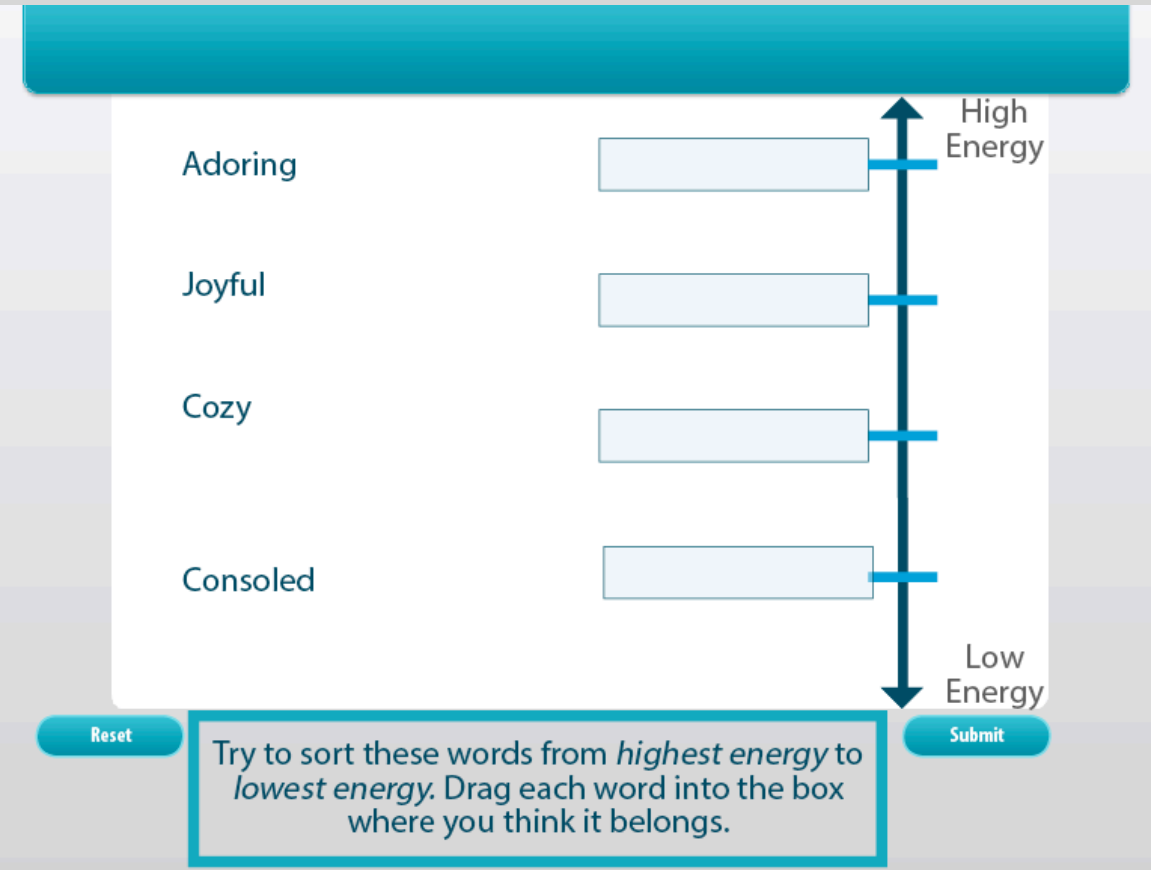
Back

Next

3) Understanding Emotions
   - Introduction: advantages and basic concepts
   - Tone and Energy descriptions
   - Sorting words into positive or negative tone categories
     - ANEW Word List (Bradley & Lange)
   - Sorting words into positive or negative tone dimensions
   - Sorting words into high to low energy dimension
   - Explains how to think about tone and energy
   - Sorting words in 4 quadrants (tone, energy)
   - Blends – descriptive explanation, strategy for how to come up with blended emotion
     - Plutchik's eight primary emotions…
   - Questions – choose the correct blended emotion
   - Changes – descriptive explanation
   - Questions – choose the event that changed the person's emotion from A to B
   - Point of view – descriptive explanation, strategy for how to come up with
   - Point of view multiple choice questions
   - Conclusion



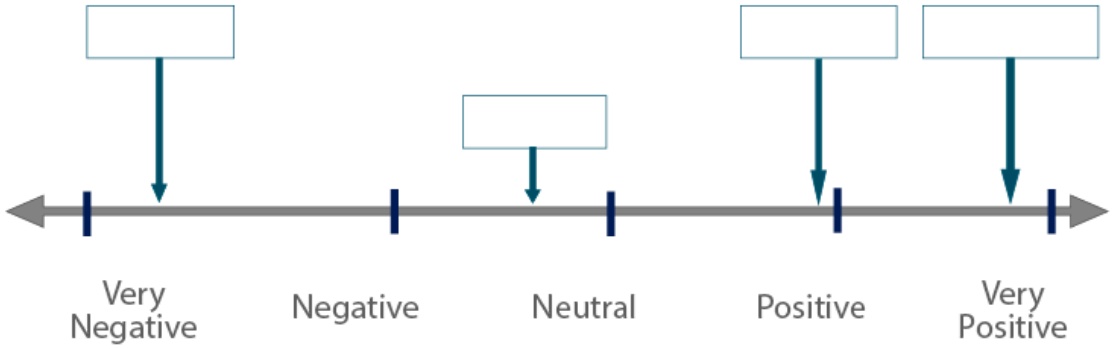

Positive
Negative
Ebullient
Tranquil
Exuberant
Optimistic
Thrilled
Dismayed
Irritated
Dejected
Great job! This is how the words should be sorted.
Next


Adoring
Joyful
Cozy
Consoled
High Energy
Low Energy
Reset
Submit
Try to sort these words from *highest energy* to *lowest energy*. Drag each word into the box where you think it belongs.

Enthusiastic Trusting

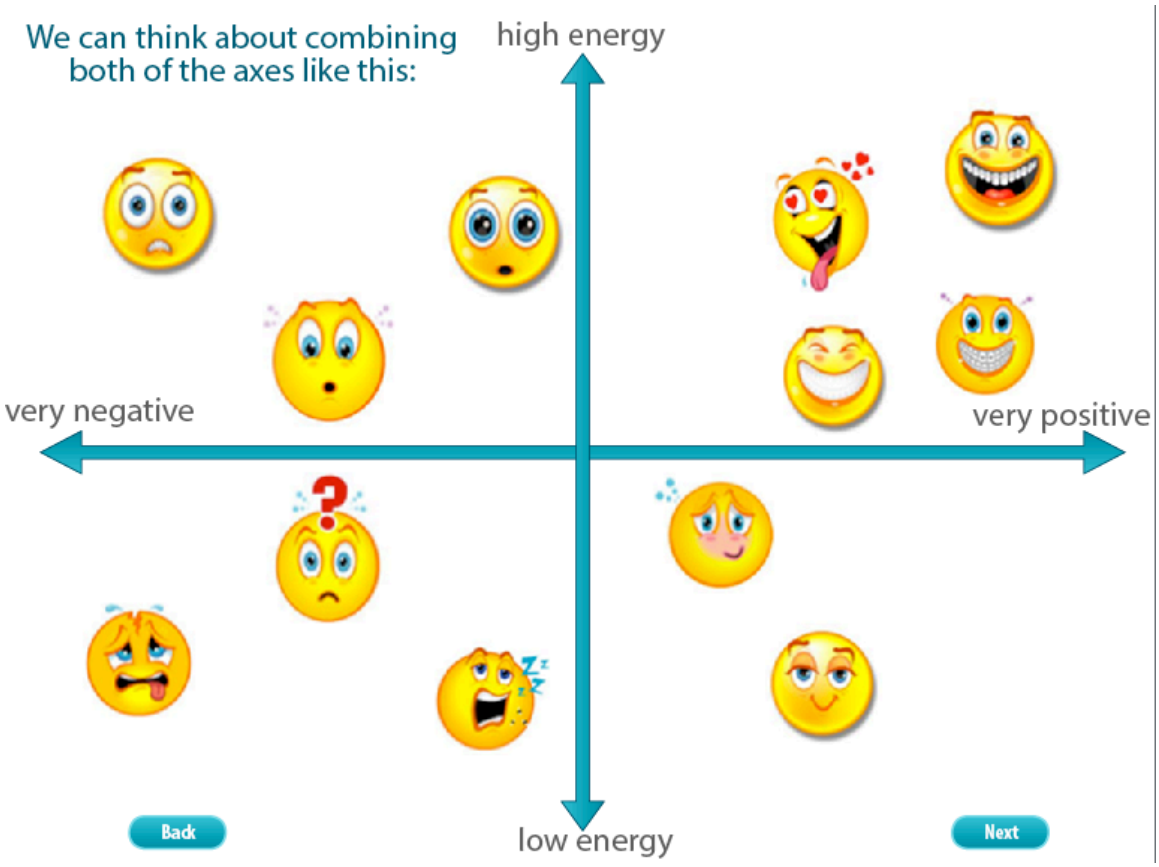
Subdued Panicked

Now let's practice. Try to sort these words based on their tone.

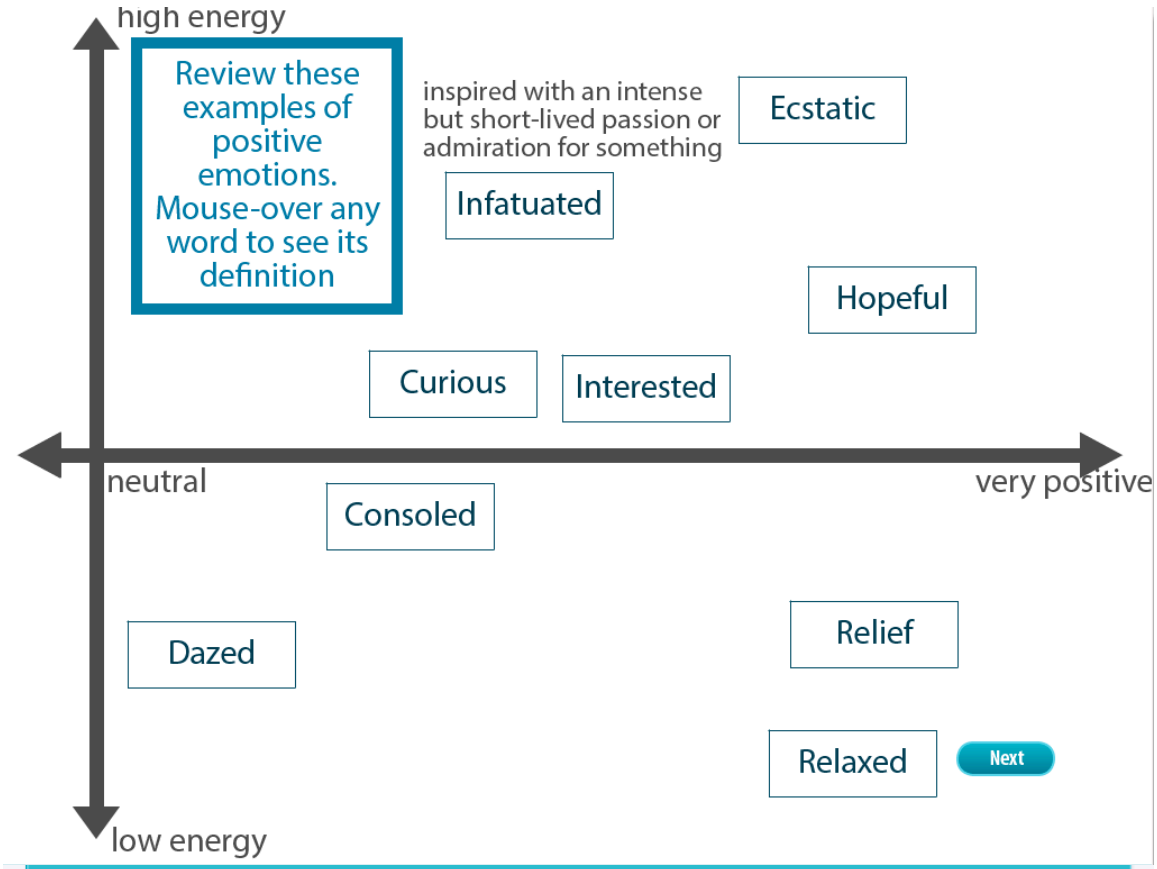


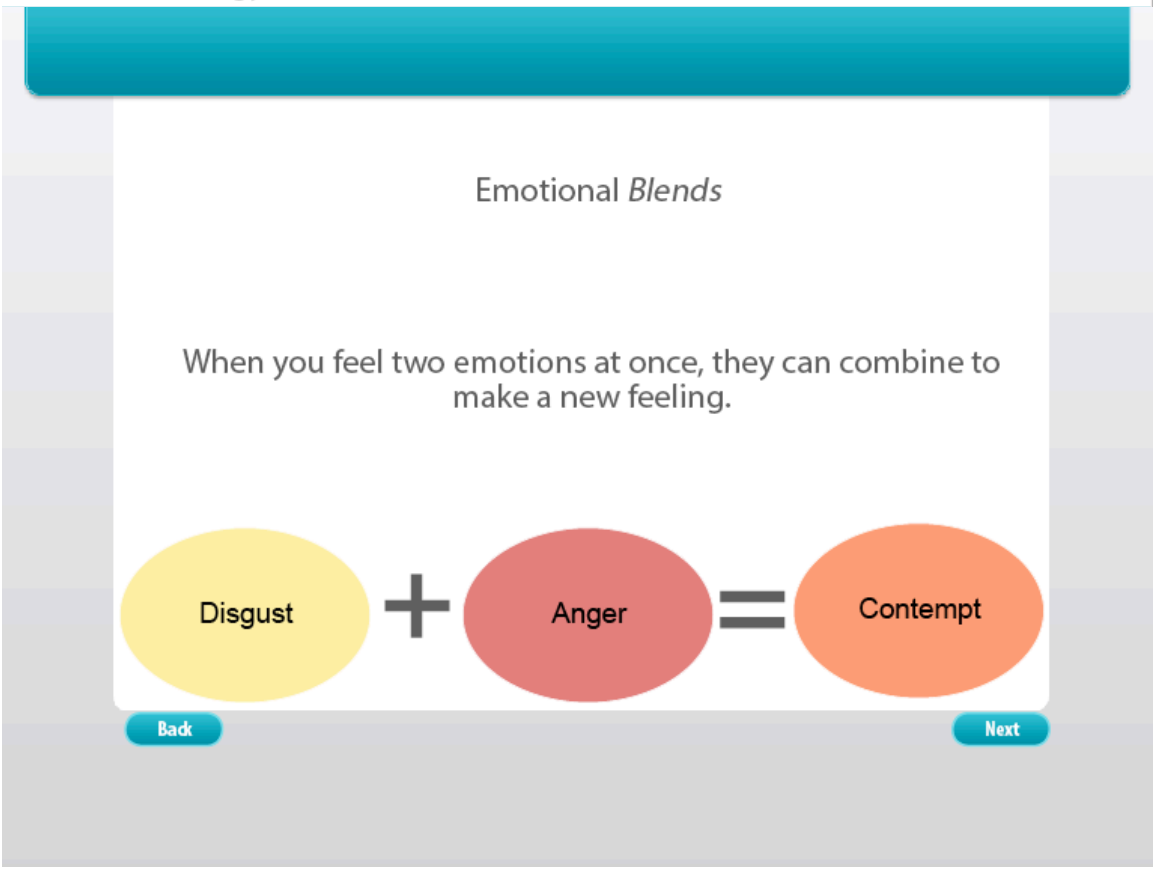
Back Reset Submit

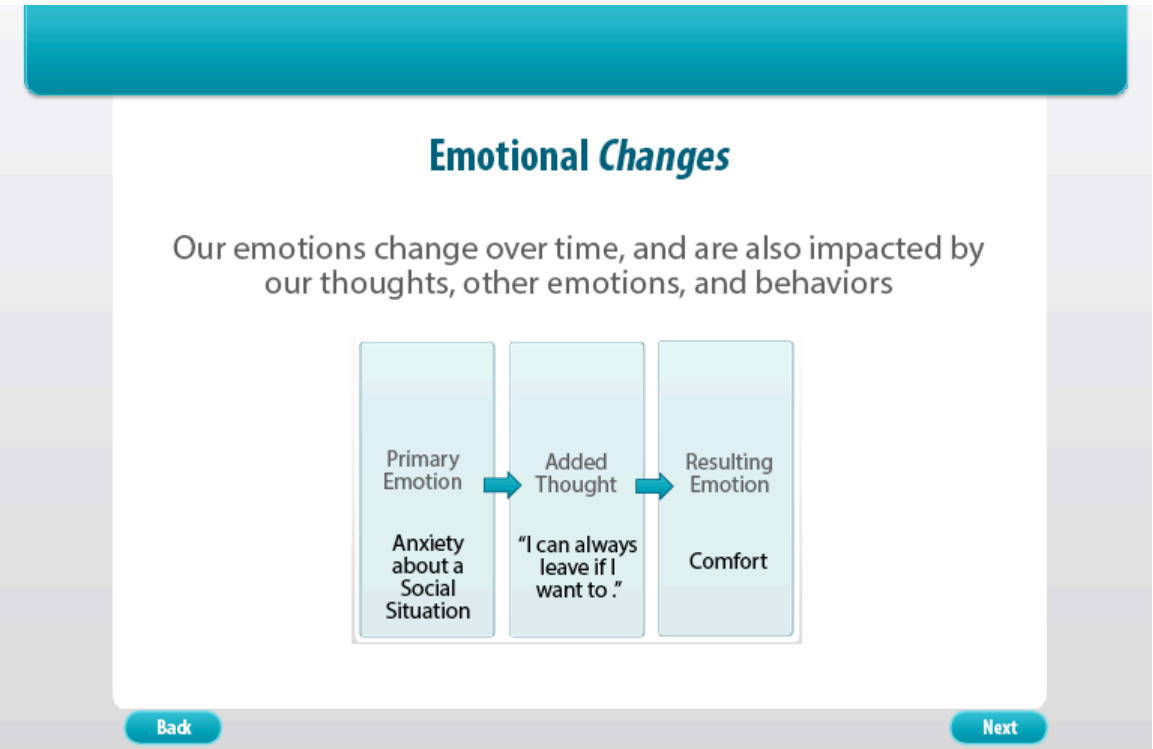
We can think about combining both of the axes like this:



Back Next


high energy
Review these examples of positive emotions. Mouse-over any word to see its definition
inspired with an intense but short-lived passion or admiration for something
Ecstatic
Infatuated
Hopeful
Curious
Interested
neutral
very positive
Consoled
Dazed
Relief
Relaxed
Next
low energy

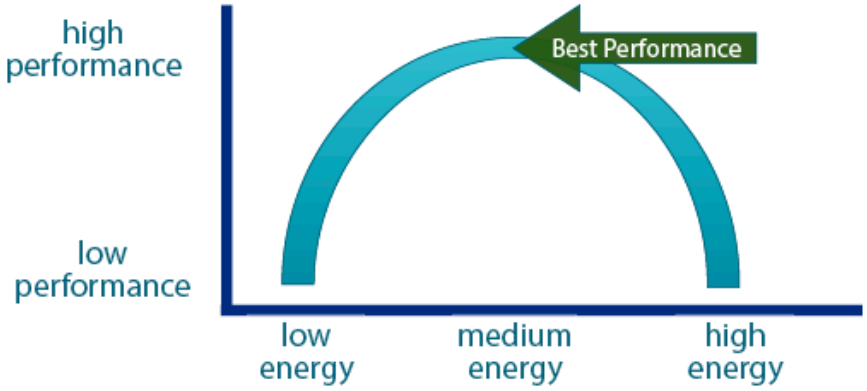

Emotional *Blends*
When you feel two emotions at once, they can combine to make a new feeling.
Disgust
+
Anger
=
Contempt
Back
Next



4) Facilitating Emotions
   - Introduction – conceptually how a helpful mood matches the tone of the task you are trying to work on

- "Energy hill" explanation
    - Yerkes, & Dodson. (1908). The relation of strength of stimulus to rapidity of habit-formation. *Journal of Comparative Neurology and Psychology, 18*, 459-482.
- Multiple choice questions – where on energy hill – scenarios
- Categorizing non-emotional words into positive/negative tone and high/low energy introduction
    - ANEW Word List (Bradley & Lange)
- Categorizing non-emotional words – 4 quadrant drag-and-drop
- Multiple choice – which emotion is this non-emotional word most like?
- Conclusion

We tend to perform best when we are in a "medium energy" state on that hill.



Back Next

Multiple Choice

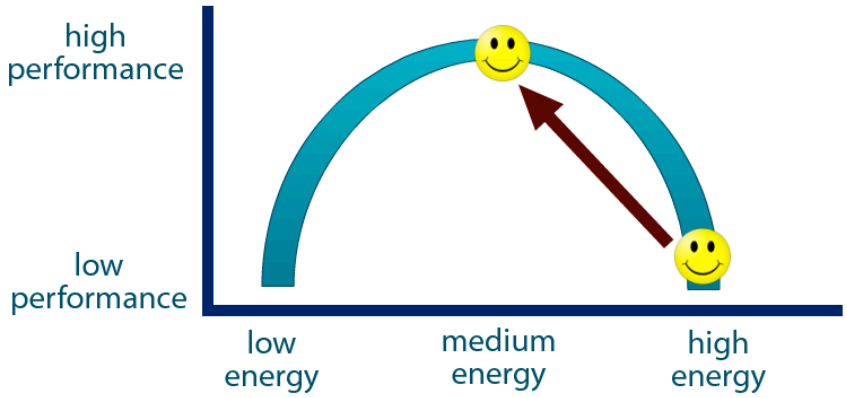
Imagine that you were overcharged for car repairs. You have tried talking to the repairman, who was not helpful. You now ask to speak to the manager.

- Enraged
- Happy
- Furious
- Irritated

Incorrect. Actually, a more neutral mood like 'irritated' will help you remain calm while you speak with the manager . Press the 'Submit' button again to continue.

Back Submit

So if you are feeling very "fired-up" (high energy), you might perform better if you switched to a lower-energy mood.

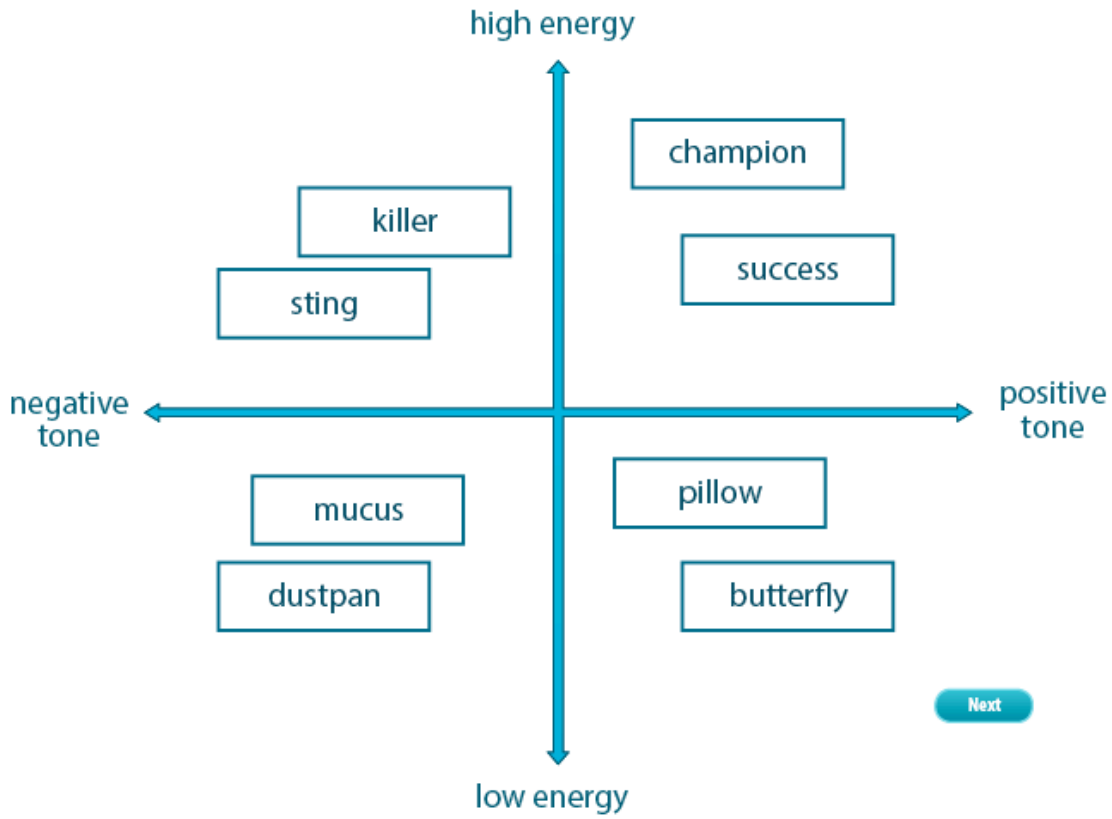


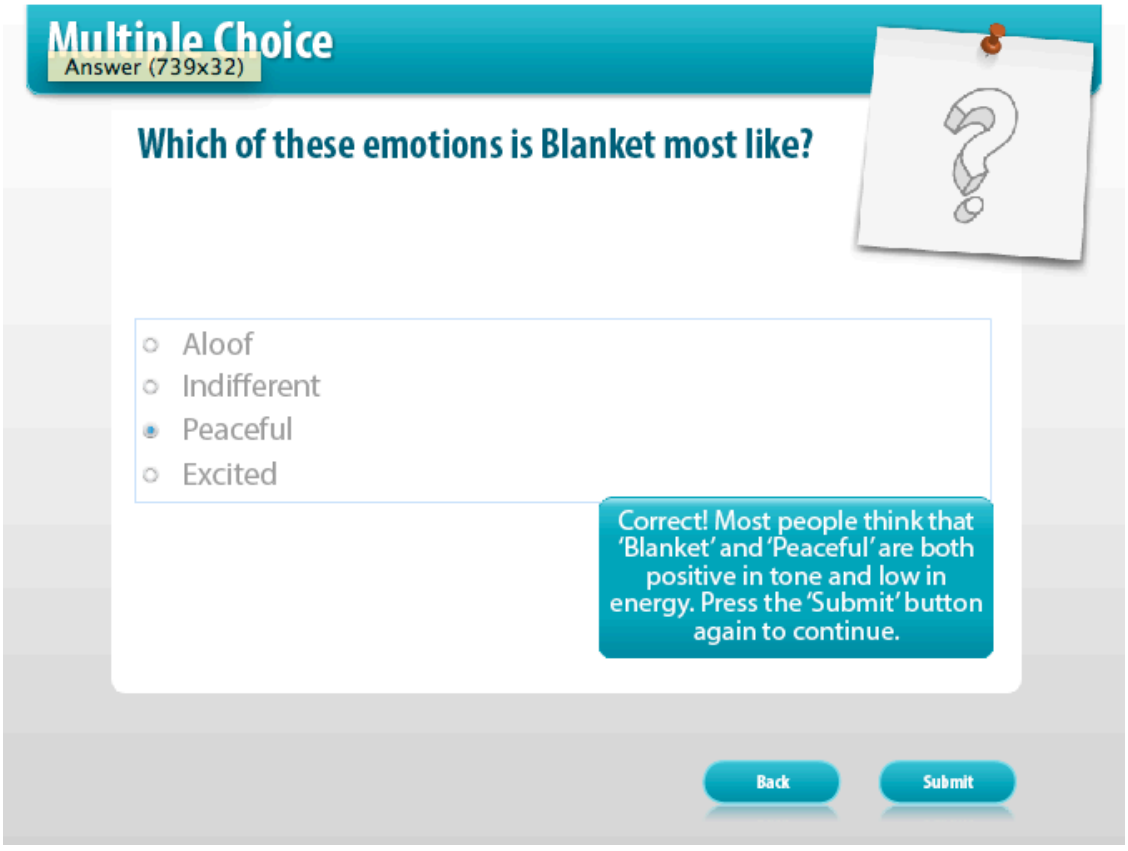
Back Next

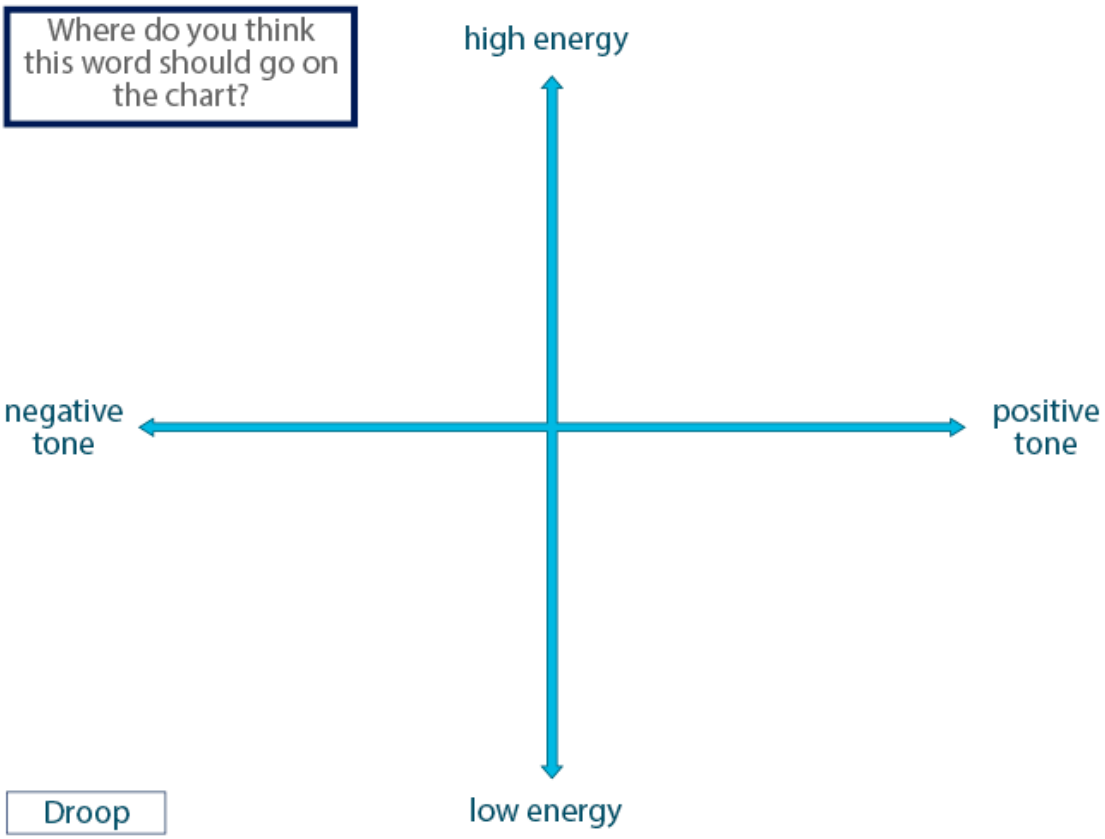
Some words are negative in tone and high in energy, like:

terrified
killer
sting
roach

Back Next


high energy
champion
killer
success
sting
negative tone
positive tone
mucus
pillow
dustpan
butterfly
Next
low energy


Multiple Choice
Answer (739x32)
Which of these emotions is Blanket most like?
Aloof
Indifferent
Peaceful
Excited
Correct! Most people think that 'Blanket' and 'Peaceful' are both positive in tone and low in energy. Press the 'Submit' button again to continue.
Back
Submit



5) Managing Emotions
   - Introduction – advantages
   - Sorting problems into easy to deal with vs difficult to deal with categories
   - Steps to dealing with a problem
   - 2 ways to deal with a problem – find a solution or change the way you think about it
   - Example scenario of character's solvable problem and how he solves it using the steps
   - Change the way you think – positive reappraisal and mindfulness intros
     - Folkman, & Lazarus. (1988). Coping as a mediator of emotion. *Journal of Personality and Social Psychology, 54*(3), 466-475.
   - Positive reappraisal explanation – bigger picture or different person's perspective
     - Schartau, Dalgleish, & Dunn. (2009). Seeing the bigger picture: Training in perspective broadening reduces self-reported affect and psychophysiological response to distressing films and autobiographical memories. *Journal of Abnormal Psychology, 118*(1), 15-27.
     - Finkel, Slotter, Luchies, Walton, & Gross. (2013). A brief intervention to promote conflict reappraisal preserves marital quality over time. *Psychological Science OnlineFirst, doi: 10.1177/0956797612474938.*
   - Example scenario of character's problem – use positive reappraisal strategy – big picture thinking and finding benefits
   - Quiz – benefit finding

- Example scenario of character's problem – use positive reappraisal strategies – perspective taking
- Quiz – multiple choice questions about scenario that requires positive reappraisal
- Mindfulness
    - Garland, Gaylord, & Park. (2009). The role of mindfulness in positive reappraisal. *Explore (NY)*, *5*(1), 37-44.
    - Grossman, Niemann, Schmidt, & Walach. (2004). Mindfulness-based stress reduction and health benefits: A meta-analysis. *Journal of Psychosomatic Research, 57*(1), 35-43.
- Mindfulness 3-part breath
- Mindfulness observing/accepting your body sensations
- Mindfulness observing your thoughts
- Mindfulness exercise – view pictures and notice thoughts/feelings
- Example scenario of character's problem – use positive reappraisal strategy, mindfulness, and problem-solving
- Conclusion

The advantages of being able to manage your emotions

Learning how to manage your emotions is important because it can keep you from getting too worked up or upset about a problem.

Most of the time you can either change the problem or change how you think about it.

Back Next

Drag and drop the problems into the following groups

Easy to deal with	Difficult to deal with
You missed the last bus	Your cat disappeared
There is always a traffic jam on the shortest route to work	Your friend moves far away for a better job
There's no milk in the fridge	Your significant other wants to end your relationship

Notice how the "easy to deal with" problems can be easily solved.

- For instance, if you miss the last bus, you can take a taxi or train.

The "difficult to deal with"problems take more advanced coping.

- For instance, if your cat disappears, you can try to remember your pet fondly to make yourself feel better.

Back Next

In general, there are 3 easy steps to deal with a problem.

- **Step 1:** What is the problem? Size it up!

- **Step 2:** What could I do? Look at different options!

- **Step 3:** Choose what works best!

Back Next

Step 2

Frank considers whether there is a solution to his problem or if he just has to change the way he thinks about it.

Find a solution or key to your problem.

OR

Change the way you think about your problem.

Frank thinks he may be able to come up with a solution.

Back Next

The steps of positive reappraisal

First, you have your original view.

Original View

"I am angry because it is raining."

Then, you introduce a new view that is positive.

New View

"Now I get to watch that movie I have been wanting to watch."

Then, you are left with a positive view.

More Positive View

"Today turned out to be a good day because I saw a movie."

Next

Positive Reappraisal Example

How will this affect me today?
I am upset that I didn't get into the program.

How will this affect me next month?
I may be a little upset I am not in the program.

How will this affect me next year?
I can apply again and writing the application will be easier the second time.

How will this affect me in five years?
I probably won't care that I didn't get into the program the first time.

Back

Next

Quiz: Benefit Finding

Drag the corresponding benefits that would be most helpful in achieving a positive view of the situation into the chart below.

Event	Benefits
Failed a science test	

Don't need to learn this stuff anyways

Teacher is to blame for me failing

Chance to explore new academic areas

Chance to learn new study strategies

Motivation to work harder

No reason to study because I will fail again

Submit

If you are in a situation when you cannot talk to a friend or relative about your problem, try to imagine what they would tell you.

Back

Next

Positive Reappraisal Example

Event	Benefits
Not accepted into academic program	Applying next year will be easier because I have already gone through the application process.
	I will have more time to work on other projects this semester without having to commit time to the program.

Back Next

Mindful Breathing

- Now try to focus only on your breath going in and out.
- Try to move your breath in and out as the balloon inflates and deflates.
- Inhale through your nose and exhale through your mouth.

Back Next

Observing the body

- Now move your attention up to your torso.
- Can you feel your breath in your lower back, belly, chest, and shoulders?

Back Next

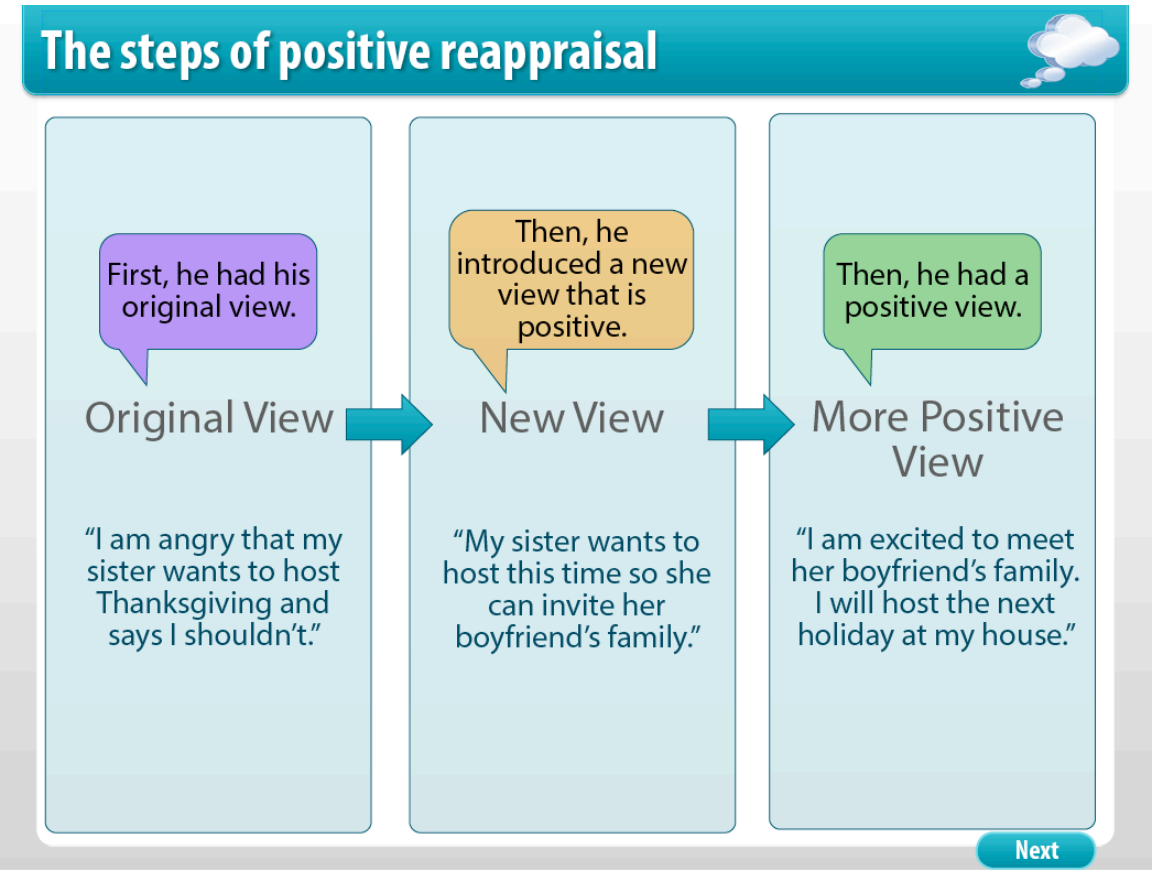
Dealing with a difficult problem

Change the way he thinks about the problem

Carl can also try to change the way he thinks about his high cholesterol levels.

Let's see what Carl thinks are the benefits of his situation...

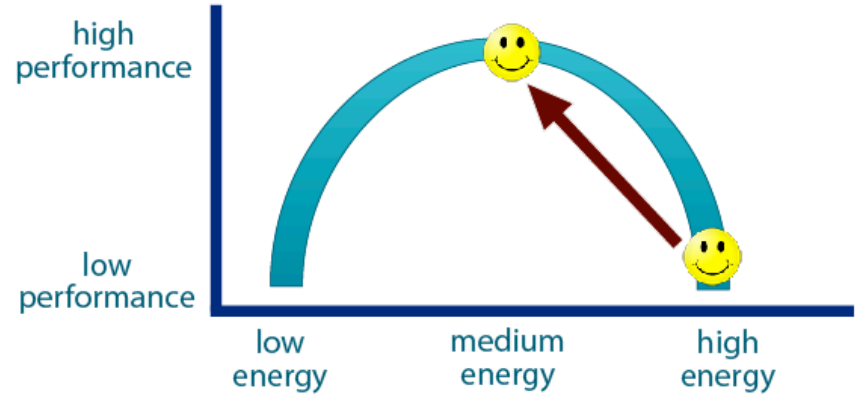
Back Next



6) Conclusion
   - Introduction
   - Review of perceiving
   - Review of facilitating
   - Review of understanding
   - Review of managing
   - Scenarios with characters incorporating all of the lessons
   - Final review

Final Review

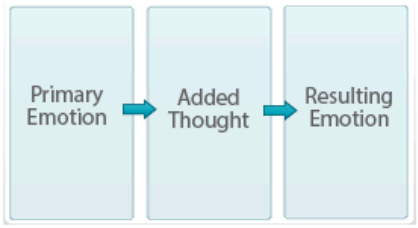
You have learned the importance of controlling your energy level to perform different tasks.

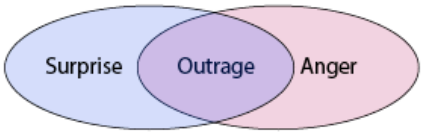


Back Next

Final Review

You have learned how emotions combine and progress over time.

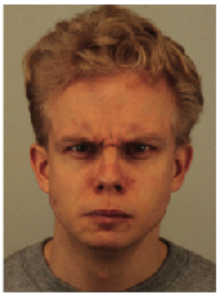




Back Next

Final Review

You have learned to focus on the eyes and mouth when reading emotional expressions on faces. You have also learned what to look for specifically when identifying specific emotions.



Back Next

Final Review

You have learned how to approach difficult problems.

Find a solution or key to your problem.

Change the way you think about your

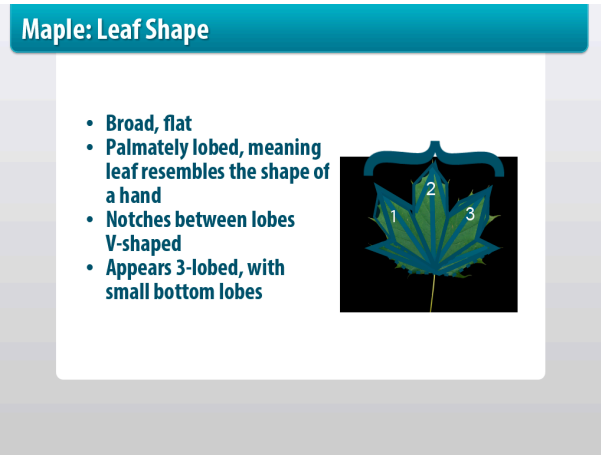
Back Next

External Awareness

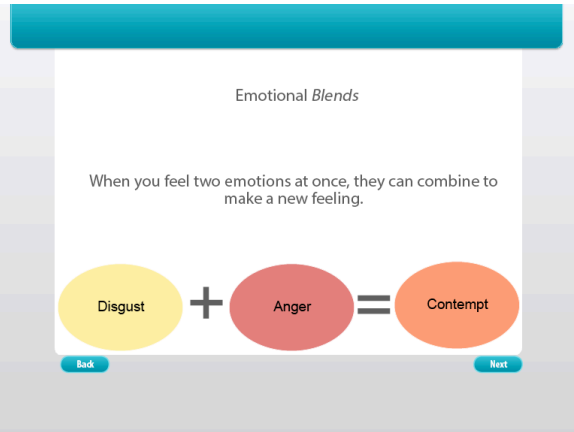
A matched set of training materials has also been developed to serve as a non-emotion-focused control condition. The materials are matched in length, difficulty, and general time requirements, but focus the participant on awareness of the external environment. The modules are matched along the same dimensions as the emotionally based Internal Awareness, including Perceiving, Understanding, Facilitating, and Managing. The pages that follow show a sample of screen images depicting some of the content of these control modules:

Active Treatment: Perceiving Emotions

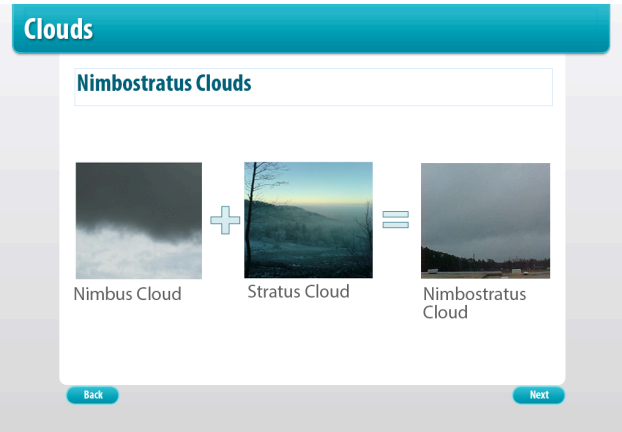
Placebo Control: Perceiving Plants



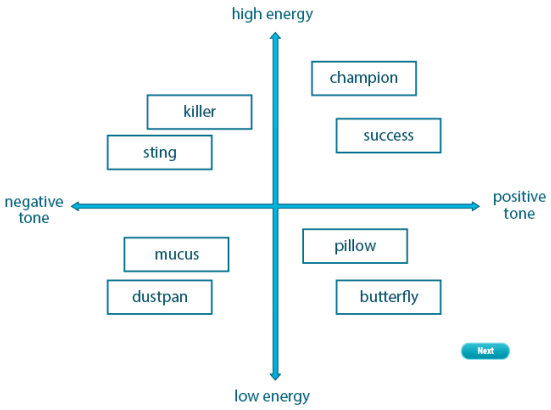
Active Treatment: Understanding Emotions



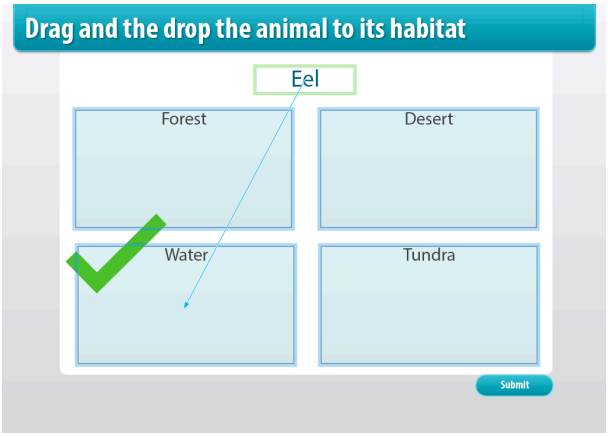
Placebo Control: Understanding Weather



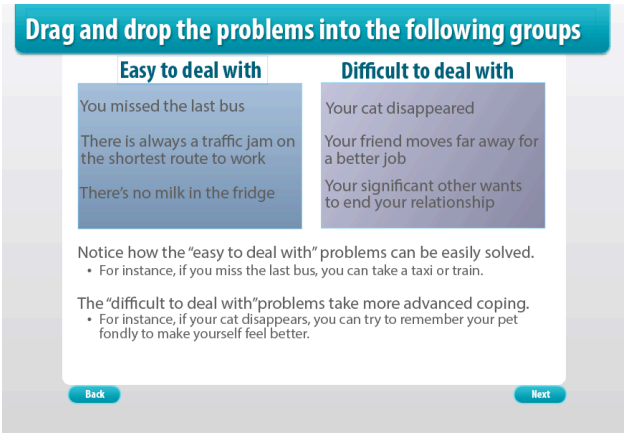
Active Treatment: Facilitating Emotions



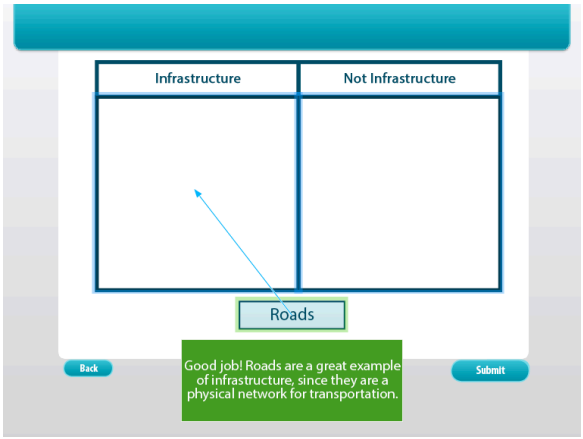
Placebo Control: Animals



Active Treatment: Managing Emotions



Placebo Control: Infrastructure Awareness



KEY RESEARCH ACCOMPLISHMENTS:

INITIAL NEUROIMAGING STUDY-

- 70 participants have been enrolled, and the study is closed to new enrolment.
- 65 participants have completed scanning/study procedures, providing usable data.
- Data analysis is ongoing.
- 22 posters based on preliminary findings have been presented at professional conferences during this report period, and 66 presented overall during the course of the study.

MODIFICATION: DEVELOPMENT OF EI TRAINING PROGRAM-

- All materials have been researched, developed, proofread, and programmed into the web-presentation system.
- A secure web-server has been established.
- The local McLean IRB protocol has been approved.

REPORTABLE OUTCOMES:

INITIAL NEUROIMAGING STUDY

- 7 posters were presented McLean Hospital Research Day, January 16, 2013 in Belmont, MA.
- 1 poster was presented at the international Conference on Applications of Neuroimaging to Alcoholism
- 6 posters were presented at the 68th Annual Scientific Meeting of the Society of Biological Psychiatry in San Francisco, CA, May 16-18, 2013.
- 5 posters were presented at the 27th Annual Meeting of the Associated Professional Sleep Societies in Baltimore, MD, June 1-5, 2013.
- 15 manuscripts (attached and listed below) were accepted and/or published in scientific journals:

1. **Killgore, WD**, Weber, M, Schwab, ZJ, DelDonno, SR, Kipman, M, Weiner, MR, & Rauch, SL. Grey matter correlates of trait and ability models of emotional intelligence. Neuroreport 23, 551-555, 2012.

2. **Killgore, WD**, Schwab, ZJ, Kipman, M, DelDonno, SR, Weber, M. Voxel-based morphometric grey matter correlates of daytime sleepiness. Neurosci Lett, 518(1), 10-13, 2012.

3. **Killgore, WD**, Schwab, ZJ, & Weiner, MR. Self-reported nocturnal sleep duration is associated with next-day resting state functional connectivity. Neuroreport, 23, 741-745, 2012.

4. **Killgore, WD**, & Schwab, ZJ. Sex differences in the association between physical exercise and cognitive ability. Perceptual and Motor Skills, 115, 605-617, 2012.

5. Kipman, M, Weber, M, Schwab, ZJ, DelDonno, SR, & **Killgore, WD**. A funny thing happened on the way to the scanner: Humor detection correlates with gray matter volume. Neuroreport, 23, 1059-1064, 2012.

6. **Killgore, WD**, Schwab, ZJ, Weber, M, Kipman, M, DelDonno, SR, Weiner, MR, & Rauch, SL. Daytime sleepiness affects prefrontal regulation of food intake. NeuroImage, 71, 216-223, 2013.

7. **Killgore, WD**, Schwab, ZJ, Kipman, M, DelDonno, SR, & Weber, M. Insomnia-related complaints correlate with functional connectivity between sensory-motor regions. Neuroreport, 24, 233-240, 2013.

8. Webb, CA, Schwab, ZJ, Weber, M, DelDonno, SR, Kipman M, Weiner, MR, & **Killgore WD**. Convergent and divergent validity of integrative versus mixed model measures of emotional intelligence. Intelligence, 41, 149-156, 2013.

9. Weber, M, Webb, CA, DelDonno, SR, Kipman, M, Schwab, ZJ, Weiner, MR, & **Killgore, WD**. Habitual 'Sleep Credit' is associated with greater gray matter volume of the medial prefrontal cortex, higher emotional intelligence, and better

mental health. Journal of Sleep Research, 22, 527-534, 2013.

10. **Killgore, WD**, Schwab, ZJ, Tkachenko, O, Webb, CA, DelDonno, SR, Kipman M, Rauch SL, and Weber M. Emotional intelligence correlates with functional responses to dynamic changes in facial trustworthiness. Social Neuroscience, 8, 334-346, 2013.

11. **Killgore, WD**, Weber, M, Schwab, ZJ, Kipman, M, DelDonno, SR, Webb, CA, & Rauch, SL. Cortico-limbic responsiveness to high-calorie food images predicts weight status among women. International Journal of Obesity (in press).

12. **Killgore, WD**. Self-reported sleep correlates with prefrontal-amygdala functional connectivity and emotional functioning. Sleep (in press).

13. **Killgore WD**, & Gogel, H. The Design Organization Test (DOT): Further Demonstration of Reliability and Validity as a Brief Measure of Visuospatial Ability. Applied Neuropsychology: Adult (in press).

14. Cohen-Gilbert, JE, **Killgore, WD**, White, CN, Schwab, ZJ, Crowley, DJ, Covell, MJ, & Silveri, MM. Differential influence of safe versus threatening facial expressions on decision-making during an inhibitory control task in adolescence and adulthood. Developmental Science (in press).

15. **Killgore, WD**, Kipman, M, Schwab, ZJ, Tkachenko, O, Preer, L, Gogel, H, Bark, JS, Mundy, EA, Olsen, EA, & Weber, M. Physical exercise and brain responses to images of high calorie food. Neuroreport (in press).

MODIFICATION: DEVELOPMENT OF EI TRAINING PROGRAM-

- Subject recruitment has not yet been initiated. McLean IRB approval has been granted, and we are currently awaiting approval from the US Army HRPO.

CONCLUSION:

We have completed data collection on 70 participants, yielding complete and usable data sets from 65 participants. The study is closed to further enrollment but remains open for data analysis only. Data quality checks and preprocessing have been completed and data analysis is currently underway.

Since the start of funding for this project 3 years ago, we have published/presented 66 abstracts, posters, and oral presentations at various scientific conferences and have already successfully published 15 manuscripts in peer-reviewed journals, with numerous others in submission and in preparation. Several of these initial findings have already received wide-spread attention in the scientific press and popular media, including write-ups in the Los Angeles Times (http://articles.latimes.com/2011/jun/14/news/la-heb-sleep-carbs-20110614), Chicago Tribune (http://articles.chicagotribune.com/2012-04-25/health/sc-health-0425-bit-of-fit-

20120425_1_junk-food-unhealthy-food-high-calorie-foods), and stories on several television news programs. Our manuscript on functional connectivity the most read article on the NeuroReport website (http://journals.lww.com/neuroreport/pages/default.aspx) for nearly two months. This same article was also selected to be the cover image and cover story to the same issue of the journal. Our recent paper on sex differences in the relationship between exercise and intelligence was also selected for press release as well (http://www.amsci.com/exercise-tied-to-higher-iq-in-women/).

The modification to the SOW has added an additional year to this project in order to develop an EI Training Program. The modification is proceeding as planned. All training materials have been developed and uploaded onto the secure web-server. The human use documents have been prepared. Subject recruitment will begin as soon as HRPO approval has been obtained.

REFERENCES:

1. Mayer JD, Salovey P, Caruso DR. Emotional intelligence as zeitgeist, as personality, and as mental ability. Bar-On R, Parker JD, editors. San Francisco: Jossey-Bass; 2000.
2. Mayer JD, Caruso DR, Salovey P. Emotional intelligence meets traditional standards for an intelligence. Intelligence. 1999;27:267-98.
3. Mayer JD, Salovey P, Caruso DR, Sitarenios G. Emotional intelligence as a standard intelligence. Emotion. 2001;1(3):232-42.
4. Bar-On R, Tranel D, Denburg NL, Bechara A. Exploring the neurological substrate of emotional and social intelligence. Brain. 2003;126(Pt 8):1790-800.

APPENDICES:

Page

List of Assessments…… **52**
Note: As the study is closed to recruitment, a list of the assessments is included in this report rather than a copy of each assessment.

Quad Chart …… **54**

Abstracts…… **114**

Manuscripts…..…..…… **125**

Appendix: List of Assessments

1. Pre-Scan Information Questionnaire (PSIQ)
2. Mayer-Salovey-Caruso Emotional Intelligence Test (MSCEIT V2.0)
3. Bar-On Emotional Quotient Inventory (EQi)
4. Self-Rated Emotional Intelligence Scale (SREIS)
5. Memory Suppression Task Training (2-4 Trials)
6. Memory Suppression Phases: A, B, C
7. Positive and Negative Affect Schedule (PANAS)
8. Memory Suppression Task-Suppression (4^{th} phase) (MST1)
9. Memory Suppression Recall (MST2; NO SCANNING)
10. Memory Suppression Task-Face Interference (MST3)
11. Memory Suppression Task-Scene Interference (MST4)
12. Emotional Distraction Task (EDT)
13. Social Dominance Task (SDT)
14. Food Perception Task (FPT)
15. Food/Activity Decision Task (FDT)
16. BMAT Anger
17. BMAT Fear
18. BMAT Happy
19. BMAT Trustworthy
20. Overt Trustworthiness Task (OTT)
21. Resting fMRI
22. Memory Suppression Task Post Test
23. Emotion Distraction Post Test
24. Masked Affect Post Test
25. Food Recognition Post Test
26. Food Ratings
27. Barratt Impulsivity Scale (BIS11)
28. Connor-Davidson Resilience Scale (CD-RISC)
29. Invincibility Belief Index (IBI)

30. Evaluation of Risks Questionnaire (EVAR)
31. Brief Sensation Seeking Scale (BSSS)
32. Happy Chimeric Test (CFT)
33. Sad Chimeric Test (CFT)
34. Balloon Analogue Risk Task (BART)
35. Ekman 60 Face Test (60 FT)
36. Wechsler Abbreviated Scale of Intelligence (WASI)
37. Karolinska Airport Trustworthiness Test (KATT)
38. Intuition Test
39. Facial Assessment of Trustworthiness Test (FATT)
40. Design Organization Test (DOT) – FORM A and B
41. Iowa Gambling Task (IGT)
42. Revised NEO Personality Inventory (NEO-PI-R)
43. Anxiety Sensitivity Index (ASI)
44. Morningness-Eveningness Questionnaire (MEQ)
45. Courtauld Emotion Control Scale (CECS)
46. Beck Depression Inventory (BDI)
47. Trust Go/NoGo (Form A or X)/Trust Go/NoGo Reversed (Form B or Y)
48. Personality Assessment Inventory (PAI)
49. Humor Appreciation Test (HAT)
50. Global Assessment Tool (GAT)
51. WRAT-3 Reading Assessment
52. Intolerance of Uncertainty Scale
53. Toronto Alexithymia Scale (TAS-20)
54. Social Discounting Task
55. Trait Meta-Mood Scale
56. Emotion Regulation Questionnaire
57. Reading the Mind in the Eyes Task
58. Empathy Quotient Index
59. Beck Anxiety Index (BAI)
60. Mindful Attention Awareness Scale

The Neurobiological Basis and Potential Modification of Emotional Intelligence through Affective / Behavioral Training

W81XWH-09-1-0730

PI: William D. Killgore, Ph.D. **Org:** McLean Hospital

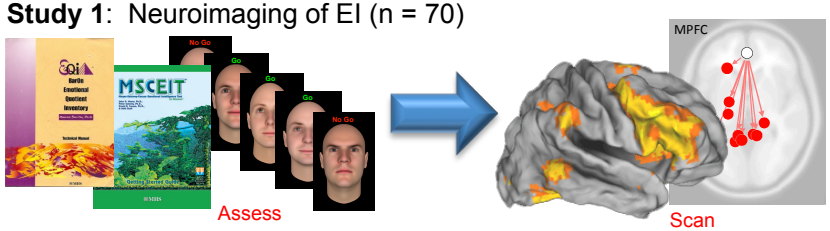
Study/Product Aim(s)

- Validate the two major theories of Emotional Intelligence (EI-Ability vs. Trait) using behavioral testing and neuroimaging.
- Quantify the association between major EI instruments and actual behavioral skills associated with emotional processes.
- Identify the specific brain regions, structures, and systems involved in EI.
- Develop a pilot training program for improving EI capacities.

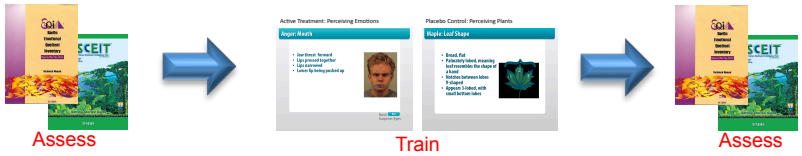
Approach

Two studies: 1) Cross-sectional neuroimaging study of 70 participants who complete EI assessments, emotion tests, and undergo functional and structural neuroimaging; 2) Development of a 6 module EI training program based on scientific data, which will be evaluated against a placebo training program in a between group longitudinal pre-post testing design in 60 participants.

Study 1: Neuroimaging of EI (n = 70)



Study 2: Training of EI (n = 30 Tx; n = 30 placebo)



Accomplishments: Study 1 is complete and has resulted in over 15 published manuscripts & 66 conference presentations. Study 2 preparations are complete and data collection will commence once HRPO approval has been granted.

Activities CY	09	10	11	12	13	14
Study preparations: Study 1						
Data collection: Study 1						
Analysis/dissemination: Study 1						
Study preparations: Study 2						
Data collection: Study 2						
Analysis/dissemination: Study 2						
Estimated Budget ($xxxK)	**10K**	**132K**	**132K**	**140K**	**69K**	**69K**

Goals/Milestones

CY10 Goal – Study 1 preparations, human subjects approval, start study recruitment and data collection

☑ Completed study preparations early, started data collection early

CY11 Goals – Data collection, quality checks

☑ Test approximately 20 subjects per CY

CY12 Goal – Complete Data collection/analyze and publish findings

☑ Study 1 data collection completed

☑ Obtain 6 month no-cost extention

☑ Data analyzed; 15 papers published; 66 conference presentations

CY13 Goal –Study 2 SOW Modification to develop training program

☑ Modification approved;

☑ All training programs developed & ready; awaiting HRPO approval

☐ Run 60 sx through EI/placebo training with pre-post assessments

Updated: 24 OCT 2013

2013 Abstracts:

Sex Differences in the Association Between Sleep and Intelligence

Olga Tkachenko, Zachary J. Schwab, Maia Kipman, Sophie DelDonno, Hannah Gogel, Lily Preer, & William D.S. Killgore

Social, Cognitive & Affective Neuroscience Laboratory, McLean Hospital, Harvard Medical School

The role of sleep in cognitive functioning remains poorly understood, though some developmental evidence implies that higher intellectual capacity may be associated with a decreased need for sleep. This study explored the relationship between habitual sleep and cognitive functioning in an adult population, focusing on differences between men and women.

55 healthy volunteers, aged 18 to 45 (mean age 29.8±7.9; 28 males) were administered the Wechsler Abbreviated Scale of Intelligence (WASI). Additionally, participants completed the Epworth Sleepiness Scale (ESS) and a questionnaire about their sleep habits. The Full Scale IQ on the WASI was correlated with the average number of hours of sleep on typical week- and weekend nights, with age, education, and Socioeconomic Status (SES) as covariates.

A significant negative correlation was observed between IQ scores and the average amount of sleep on both week- and weekend nights ($p<0.01$). Analysis by gender reveals that this correlation is significant only in females. These relationships remained significant when controlling for ESS scores and the amount of sleep obtained the night prior to administration of the WASI.

Findings suggest that females with greater intellectual ability require less sleep. Two possible explanations exist for this effect. The first supports the Neural Efficiency hypothesis, indicating that individuals with higher cognitive functioning may also display higher efficiency in neuronal recovery during sleep. The other suggests that individuals with shorter sleep duration benefit from a longer period of wakefulness and greater opportunity for cognitive stimulation. Several key aspects may account for the gender disparity: previously identified differences in brain morphology, particularly the role of white and gray matter in intellectual functioning; differences in levels of hormones, such as testosterone; as well as societal and cultural pressures specific to each gender, which may play into the differences in sleep habits and cognitive functioning.

Abstract presented at the McLean Hospital Research Day, January 16th, 2013.

Validation of the Design Organization Test (DOT) in a Healthy Population

Hannah Gogel, Sophie DelDonno, Maia Kipman, Lily A. Preer, Zachary J. Schwab, Olga Tkachenko, William D.S. Killgore

Social, Cognitive & Affective Neuroscience Laboratory, McLean Hospital, Harvard Medical School

A great deal of effort has been put into decreasing the duration of various neuropsychological measures in order to reduce patient fatigue and administration costs. The Design Organization Test (DOT; Killgore et al., 2005) was developed as a time-efficient alternative for the Block Design (BD) task that is a key subtest of the Wechsler Intelligence Scales. The DOT is a 2-minute paper-and-pencil task designed to assess visuospatial abilities. Participants use a coded key of block images to replicate images of various designs within a grid of squares. Although the DOT has been validated among clinical neurological patients, we sought to verify the reliability of the DOT in a healthy, more diverse population.

Two alternate versions of the DOT and the Wechsler Abbreviated Scale of Intelligence (WASI) were administered to sixty-one healthy participants between the ages of 18 and 45. Correlations were calculated to assess the reliability of both forms of the DOT.

Both forms of the DOT were found to correlate with the WASI BD task ($r = .756$, $p < .001$). The alternative forms of the DOT correlated highly with each other ($r = .802$, $p < .001$) regardless of the order of administration (Fisher's r-to-z transformation, $z = -.609$, ns.).

These data, along with previous work (Killgore et al., 2005), suggest that the DOT is a reliable and valid visuospatial measure in clinical and healthy populations. It is also possible for the DOT to be used as an equivalent alternative to the Block Design subtest of the WASI, allowing administrators to save time during a complete assessment of intelligence. The potential for verbal administration of this task could lead to use with a broader variety of patients.

Abstract presented at the McLean Hospital Research Day, January 16th, 2013.

Emotional Intelligence as a Mediator of the Association between Anxiety Sensitivity and Anxiety Symptoms

Lily A. Preer, Olga Tkachenko, Hannah Gogel, Zachary J. Schwab, Maia Kipman, Sophie R. DelDonno, Mareen Weber, Christian A. Webb, William D.S. Killgore

Social, Cognitive & Affective Neuroscience Laboratory, McLean Hospital, Harvard Medical School

The construct of Anxiety Sensitivity (AS), which refers to the fear of the physical sensations, thoughts, and social consequences associated with anxiety, has been theorized to be a cognitive vulnerability that contributes to the development of an anxiety disorder. However, some evidence suggests that certain emotional factors may affect this relationship. We hypothesized that the level of Emotional Intelligence (EI) would mediate the relationship between AS and self-rated anxiety symptoms.

Sixty-one healthy adults (30 men) aged 18 to 45 (mean age 30.42 ±8.14) completed measures of AS (Anxiety Sensitivity Index, ASI), anxiety symptoms (Personality Assessment Inventory, PAI), a "trait" measure of EI (Bar-On Emotional Quotient Inventory, EQ-i), and two "ability" measures of EI (Mayer-Salovey-Caruso Emotional Intelligence Test, MSCEIT; SelfRated Emotional Intelligence Scale, SREIS). Mediation analyses were used to assess the influence of each of the measures of EI on the relationship between AS and anxiety symptoms.

Results: EQ-i was a significant partial mediator of the relationship between AS and PAI anxiety symptoms ($z=2.95$, $p=.003$). However, there were no mediation effects for the ability measures of EI, either for MSCEIT scores ($z=.61$, $p=.539$) or SREIS ratings ($z=.55$, $p=.583$), on the relationship between AS and anxiety symptoms.

Conclusion: Results showed that trait EI, but not ability EI, mediated the relationship between anxiety sensitivity and anxiety symptoms. Whereas the EQ-i measures a broad range of EI traits, which overlap with general emotional wellbeing, the MSCEIT and SREIS assess specific emotional skills. These findings suggest that factors related to emotional wellbeing, rather than specific emotional skills and abilities, mediate the relationship between anxiety sensitivity and anxiety symptoms. This may have implications for interventions designed to reduce anxiety by targeting the mediating factors.

Abstract presented at the McLean Hospital Research Day, January 16th, 2013.

Abstract accepted for presentation at the 68th Annual Scientific Meeting of the Society of Biological Psychiatry, San Francisco, CA, May 16-18, 2013.

The Contributions of Emotional Intelligence and Facial Perception to Social Intuition

Sophie DelDonno, Maia Kipman, Zachary J. Schwab, & William D. S. Killgore.

Social, Cognitive & Affective Neuroscience Laboratory, McLean Hospital, Harvard Medical School

Intuition can be defined as a quick, a-logical, subconscious process that enables an individual to accurately extract information from a situation, depending on the amount of previous exposure in that domain. Intuition may be a component of emotional intelligence (EI), which is the ability to perceive, manage, and understand emotions and use that information to enhance cognition and achieve goals. Previous work has suggested that EI may play a larger role than executive function in intuitive decisionmaking tasks, perhaps because EI and intuition capacities both recruit the "somatic marker" neurocircuitry. In the present study, we studied the influence of EI on a social intuition-based decision-making task. We aimed to identify factors that contribute to the ability to intuitively learn a nonexplicit rule for categorizing faces. We hypothesized that EI accounts for a greater proportion of the variance in social intuition than the ability to simply identify emotional facial expressions. Sixty-two healthy volunteers (ages 18– 45, M=30.2, SD=8.1; 31 females) completed the Mayer-Salovey-Caruso Emotional Intelligence Test (MSCEIT), the Ekman 60 Faces Test (EFT), and an Intuition Task. The stimuli in the intuition task were taken from 300 computer-generated faces previously rated along 14 traits. These traits were reduced to a single dimension using Principal Components Analysis and the top and bottom 100 images were selected for the task. Without explicit explanation of the trait dimension, participants decided whether each face was high or low on the undefined attribute. Participants were provided with feedback on the accuracy of their responses in order to learn to facilitate learning. In a stepwise regression, total MSCEIT score emerged as a better predictor ($\beta = .401$, $p = .001$) of performance on the Intuition Task than EFT score ($\beta = .188$, $p = .15$). After dividing the MSCEIT into its four subscores and entering all variables into a linear regression, the Understanding subscore accounted for the most variance in the Intuition Task ($\beta = .536$, $p < .001$). EI predicted performance on the Intuition Task better than a test of emotional facial expression discrimination. This suggests that successful intuitive judgment of faces may require the subtle and complex skills encompassed by EI, to a greater extent than the ability to simply identify facial expressions of emotion. Additionally, the Understanding subscore strongly predicted Intuition Task performance, suggesting that this type of intuition may partly lie in the ability to label emotions, recognize groups of emotions, and understand the transitions between emotions.

Abstract presented at the McLean Hospital Research Day, January 16th, 2013

The Neurocircuitry of Impulsive Behavior

Maia Kipman Zachary J. Schwab Sophie DelDonno William D.S. Killgore

Social, Cognitive & Affective Neuroscience Laboratory, McLean Hospital, Harvard Medical School

The proclivity to make impulsive and potentially risky choices often has detrimental effects on an individual's health and wellbeing. Risk taking and impulsivity are particularly problematic for adolescents as well as for certain psychiatric populations such as patients with borderline personality disorder. The interplay between reward and cognitive control regions in the brain is thought to underlie an individual's propensity to engage in impulsive or risky behavior. Based on prior research suggesting that the nucleus accumbens mediates reward-seeking activity while the insula mediates loss aversion, we hypothesized that connectivity between these areas and orbitofrontal regions would predict individual variance in impulsivity. Fifty-eight healthy adults (29 females) ages 18 to 45 underwent functional magnetic resonance imaging (fMRI) at 3T while resting quietly with their eyes open for 6 minutes. Outside of the scanner participants completed the Barratt Impulsiveness Scale (BIS), which measures impulsive personality traits. A resting-state functional connectivity analysis was conducted using the CONN toolbox. Seed regions were placed bilaterally in the medial orbitofrontal cortex, lateral orbitofrontal cortex, insula, and nucleus accumbens. BIS scores ranged from 44 to 95 (M=61.90, SD=10.59). Impulsivity correlated with increased functional connectivity between the medial orbitofrontal cortex and the nucleus accumbens as well as with anticorrelated connectivity between the lateral orbitofrontal cortex and the insula. Participants who scored higher on the BIS had increased positive functional connectivity between the medial orbitofrontal cortex and nucleus accumbens and increased negative connectivity between the lateral orbitofrontal cortex and insula. These findings are congruent with literature on reward circuitry and risk taking propensity, and suggest that impulsiveness is associated with greater positive intercorrelations between reward areas and simultaneous inverse relationships between visceral sensation regions and brain regions involved in behavioral regulation. This pattern of neurocircuitry responses may promote impulsive and risky decisions.

Abstract presented at the McLean Hospital Research Day, January 16th, 2013

Abstract accepted for presentation at the 68th Annual Scientific Meeting of the Society of Biological Psychiatry, San Francisco, CA, May 16-18, 2013.

Differential Influence of Safe Versus Threatening Facial Expressions on Inhibitory Control Across Adolescence and Adulthood

JE Cohen-Gilbert[1,3] , WDS Killgore[2,3], ZJ Schwab[2], DJ Crowley[1,3],MJ Covell[1], D Acharya[3], JT Sneider[1,3], MM Silveri[1,3]

[1]Neurodevelopmental Laboratory on Addictions and Mental Health, McLean Imaging Ctr;[2] Ctr for Anxiety and Depression, McLean Hosp, Belmont, MA 02478; [3]Dept Psychiatry, Harvard Med Sch, Boston, MA 02215

Inhibitory control improves throughout adolescence and into adulthood, due largely to the maturation of prefrontal cortex (PFC). Connectivity between PFC and limbic circuits critical to emotional processing also develops during this time. Thus, the impact of emotional information on response inhibition may change over the course of development. In the present study, developmental differences in response inhibition were examined using a Go No-Go task that required subjects to respond or inhibit responding based on threat or safety cues present in the expression of facial stimuli. The task included two conditions: one in which subjects were required to respond (Go) to safe faces while inhibiting responding (No-Go) to threatening faces, and a second in which subjects were asked to respond (Go) to threatening faces and inhibit responding (No-Go) to safe faces. Inhibitory control was measured as percent accuracy on No-Go trials in each condition. One hundred and twelve subjects (44 female) between 12 and 45 years of age completed this task. Subjects were subdivided into three age groups: adolescent (12-14 years, N = 33), emerging adult (18-25 years, N = 36) and adult (25-45 years, N = 43). Results showed a significant main effect of age on No-Go accuracy across conditions. Significant improvements in response inhibition were seen between the adolescent group and the two adult groups, as well as between the two adult groups. A 3(age group) x 2(face type: safe or threat) mixed-model ANOVA revealed a significant interaction between age and face type for No-Go accuracy. While the adolescent group showed no difference in performance based on facial expression, the older groups showed a significant advantage on 'safe' No-Go trials compared to 'threat' No-Go trials. These findings suggest a developmental change, in adolescence, in the influence of safe versus threatening facial expressions on inhibitory capacity. Further studies are needed to differentiate the effects of developmental changes in speeded recognition versus emotional reactivity to facial cues.

Abstract presented at the McLean Hospital Research Day, January 16th, 2013

Difficulty in Falling and Staying Asleep Linked to a Sub-Clinical Increase in Symptoms of Psychopathology

Olga Tkachenko[1], Zachary J. Schwab[1], Maia Kipman[1], Sophie R. DelDonno[1], Lily A. Preer[1], Hannah Gogel[1], Mareen Weber[12], Christian A. Webb[12], William D.S. Killgore[12]

[1]McLean Hospital, Belmont, MA, [2]Harvard Medical School, Boston, MA

Sleep problems are linked with several mental disorders, particularly depression and anxiety. We have previously shown that laboratory sleep deprivation elicits significant increases in self-reported symptoms of psychopathology. Presently, we compared the effect of self-reported difficulty falling or staying asleep on these same indices of mental health concerns. We hypothesized that sleep problems would lead to a similar profile as reported previously during sleep deprivation.

Sixty-five healthy adults (33 males), aged 18-45 (30.2±8.0), completed a Sleep Questionnaire, reporting whether and how often they experienced trouble falling and/or staying asleep, and the Personality Assessment Inventory (PAI). Scores on the PAI clinical scales were compared between participants who had sleep difficulties (n=36, 19 males) and those that did not (n=29, 14 males), and correlated with frequency of weekly sleep disturbances.

Participants who endorsed sleep difficulties scored significantly higher ($p<0.05$) than those who did not on clinical scales measuring anxiety, anxiety-related disorders, depression, and schizophrenic symptoms. Subscale findings revealed that anxiety scores were elevated for cognitive, affective, and physiological dimensions, while anxiety-related disorders were driven by the phobias subscale. Depression scores were influenced by the cognitive and physiological subscales, while the elevated scores on the schizophrenia scale were driven by greater psychotic experiences scores. Higher instances of difficulty falling asleep showed significant positive correlations ($p<0.05$, Bonferroni corrected) with somatic complaints, anxiety, anxiety-related disorders, depression, schizophrenic symptoms, and borderline features.

Difficulty falling or staying asleep was associated with elevated sub-clinical psychopathology symptoms, similar to that reported during laboratory sleep deprivation. Furthermore, the increase in self-reported symptoms was strongly linked with the frequency of sleep disturbance. Although causal direction cannot be inferred, the similarity in symptoms to that produced by experimental sleep deprivation raises the possibility that sleep disturbance may serve as an underlying risk factor for disorders such as depression and anxiety.

Abstract accepted for presentation at the 68th Annual Scientific Meeting of the Society of Biological Psychiatry, San Francisco, CA, May 16-18, 2013.

Abstract accepted for presentation at the 27th Annual Meeting of the Associated Professional Sleep Societies, Baltimore, MD, June 1-5, 2013.

Linking Sleep Initiation Trouble to Neuroticism, Emotional Control, and Impulsiveness

Lily A. Preer, Olga Tkachenko, Hannah Gogel, Zachary J. Schwab, Maia Kipman, Sophie R. DelDonno, Mareen Weber, Christian A. Webb, William D.S. Killgore

Social, Cognitive & Affective Neuroscience Laboratory, McLean Hospital, Harvard Medical School

Sleep disturbance is often linked to negative affect and plays a role in psychopathology. In addition, impulsiveness and maladaptive thought control strategies have both been associated with insomnia and lack of sleep. It was hypothesized that trouble falling asleep would be related to a high degree of neuroticism, emotional control, and impulsiveness.

Sixty-one healthy adults (31 men) aged 18 to 45 completed a questionnaire about typical sleep habits, indicating whether they had trouble falling asleep and how many minutes they took to fall asleep, the Revised NEO Personality Inventory (NEO-PI-R), the Courtauld Emotional Control Scale (CECS), and the Barratt Impulsiveness Scale (BIS). A multivariate analysis of variance (MANOVA) was used to compare groups in terms of neuroticism, emotional control, and impulsiveness, and followed up with correlational analyses between these variables.

The MANOVA was significant (p=.015), and showed that trouble sleeping was associated with greater neuroticism (p=.013), emotional control (p=.042) and impulsiveness (p=.008). Minutes to fall asleep on weekdays was significantly positively associated with neuroticism (r=.475, p<.001) and impulsiveness (r=.394, p=.002), but not emotional control (p=.196).

Neuroticism, emotional control, and impulsiveness were higher in people with trouble falling asleep than normal sleepers. Likewise, minutes to fall asleep was associated with neuroticism and impulsiveness. These findings indicate that trouble falling asleep is related to degree of characteristic negative affect, the extent to which individuals are unable to cope with their negative emotions, and impulsiveness. Findings may have implications for treatment of sleep trouble, mood disturbance, and impulsive behavior.

Abstract accepted for presentation at the 68th Annual Scientific Meeting of the Society of Biological Psychiatry, San Francisco, CA, May 16-18, 2013.

Abstract accepted for presentation at the 27th Annual Meeting of the Associated Professional Sleep Societies, Baltimore, MD, June 1-5, 2013.

Problems with Sleep Initiation and Sleep Maintenance Correlate with Functional Connectivity Among Primary Sensory Cortices

William D. S. Killgore, Zachary J. Schwab, Maia Kipman, Sophie DelDonno, Scott L. Rauch, & Mareen Weber

Social, Cognitive, and Affective Neuroscience Laboratory, McLean Hospital, Harvard Medical School

According to the hyperarousal theory of insomnia, difficulty initiating or maintaining sleep occurs as a result of increased cognitive and physiological arousal brought on by acute stressors and associated cognitive rumination, placing the individual in a perpetual cycle of hyperarousal and increased sensitivity to sensory stimulation. We tested the hypothesis that difficulty initiating or maintaining sleep would be associated with increased functional connectivity among primary sensory processing and motor planning regions.

Fifty-eight healthy adults (29 men, 29 women), between 18-45 years completed a self-report inventory about sleep onset and maintenance problems and underwent a 6-minute resting state functional MRI scan at 3T. Bilateral regions of interest (ROIs) were placed in primary visual cortex, auditory cortex, olfactory cortex, and the supplementary motor cortex and the mean processed signal timecourse was extracted and correlated with the other ROIs.

Difficulty falling asleep was associated with increased functional connectivity between the primary visual cortex and other sensory regions such as the primary auditory cortex, olfactory cortex, and the supplementary motor cortex. Primary auditory cortex also showed greater connectivity with supplementary motor cortex for those with sleep initiation problems. Problems with sleep maintenance were associated with greater connectivity between the primary visual cortex and olfactory cortex.

Consistent with the predictions of the hyperarousal model, difficulty falling asleep was associated with greater functional connectivity among primary sensory and supplementary motor cortices. Such augmented functional connectivity may contribute to sustained sensory processing of environmental stimuli, potentially prolonging the latency to sleep.

Abstract accepted for presentation at the 68th Annual Scientific Meeting of the Society of Biological Psychiatry, San Francisco, CA, May 16-18, 2013.

Abstract accepted for presentation at the 27th Annual Meeting of the Associated Professional Sleep Societies, Baltimore, MD, June 1-5, 2013.

A Couple of Hours Can Make a Difference:
Self-Reported Sleep Correlates with Prefrontal-Amygdala Connectivity and Emotional Functioning

William D. S. Killgore, Zachary J. Schwab, Maia Kipman,
Sophie DelDonno, Scott L. Rauch, & Mareen Weber

Social, Cognitive, and Affective Neuroscience Laboratory, McLean Hospital, Harvard Medical School

INTRO
Prior research suggests that sleep deprivation is associated with declines in some aspects of emotional intelligence and increased severity on indices of psychological disturbance. Sleep deprivation is also associated with reduced prefrontal-amygdala functional connectivity, potentially reflecting impaired top-down modulation of emotion. It remains unknown whether this "functional disconnect" may be observed in relation to more typical levels of sleep curtailment. We examined whether self-reported sleep duration the night before the assessment would be associated with these effects.

METHODS
Sixty-five healthy adults (33 men, 32 women), ranging in age from 18-45 years documented their hours of sleep from the previous night, completed the Bar-On Emotional Quotient Inventory (EQ-i), Mayer-Salovey-Caruso Emotional Intelligence Test (MSCEIT), Personality Assessment Inventory (PAI), and underwent resting-state functional magnetic resonance imaging (fMRI). Connectivity data were analyzed using the Functional Connectivity Toolbox for SPM8.

RESULTS
Greater self-reported sleep the preceding night was associated with higher scores on all scales of the EQ-i but not the MSCEIT, and with lower symptom severity scores on half of the psychopathology scales of the PAI. Longer sleep was also associated with stronger inverse functional connectivity between the right ventromedial prefrontal cortex and right amygdala. Moreover, greater inverse connectivity between these regions was associated with higher EQ-i and lower symptom severity on the PAI.

CONCLUSIONS
Self-reported sleep duration from the preceding night is significantly correlated with inverse prefrontal-amygdala connectivity, perceived emotional intelligence, and the severity of subjective psychological distress. More sleep was associated with higher emotional and psychological strength.

Abstract accepted for presentation at the 68th Annual Scientific Meeting of the Society of Biological Psychiatry, San Francisco, CA, May 16-18, 2013.

Abstract accepted for presentation at the 27th Annual Meeting of the Associated Professional Sleep Societies, Baltimore, MD, June 1-5, 2013.

The interrelationship between 'sleep credit', emotional intelligence and mental health – a voxel-based morphometric study

Mareen Weber and William D.S. Killgore

McLean Hospital, Harvard Medical School, Belmont, MA, USA

Sleep curtailment is common in today's society, but most people also acknowledge obtaining 'sleep credit' from time to time. This means that they not only meet their individual sleep need, but also get more sleep than they subjectively need to prevent degraded daytime performance. Given the rich data on adverse effects of insufficient sleep, one could argue that getting more sleep is better, but surprisingly, not much is known about behavioral and neuroanatomical correlates of 'sleep credit'.

Before undergoing structural magnetic resonance imaging, 55 healthy right-handed adults aged 18 to 45 (mean age = 30.74, SD = 8.13) completed a questionnaire about habitual sleep duration, minimum sleep needed before an impairment is noticed (in hours), and the Bar-On Emotional Quotient Inventory (EQ-i) and Personality Assessment Inventory (PAI). 'Sleep credit' was conceptualized as habitual sleep minus minimum sleep needed before impairment is noticed. A voxel-based morphometric whole-brain multiple regression examined structural correlates of habitual 'sleep credit' ($p < .001$, uncorrected, $k \geq 90$; nuisance covariates: age, gender, total intracranial volume), which were then used to predict perceived emotional intelligence and indices of psychopathology (Bonferroni-corrected $p < .017$).

Greater habitual subjective 'sleep credit' correlated with greater gray matter volume of clusters in the left medial prefrontal cortex (892 voxels, $T = 4.81$, MNI coordinates: $x = -6$, $y = 52$, $z = -21$) and right orbitofrontal gyrus (149 voxels, $T = 4.43$, MNI coordinates: $x = 39$, $y = 51$, $z = -18$). Extracted volume data from the medial prefrontal cortex cluster predicted greater interpersonal emotional intelligence capacities, and lower somatic complaints, symptoms of paranoia, and depression on the PAI.

These data support the medial prefrontal cortex's putative role in linking sleep and emotional functioning, but more importantly suggest that behavior and brain structure may vary with 'sleep credit'.

Abstract accepted for presentation at the 27th Annual Meeting of the Associated Professional Sleep Societies, Baltimore, MD, June 1-5, 2013.

Intelligence 41 (2013) 149–156

Contents lists available at SciVerse ScienceDirect

Intelligence

Convergent and divergent validity of integrative versus mixed model measures of emotional intelligence

Christian A. Webb [a,*], Zachary J. Schwab [a], Mareen Weber [a], Sophie DelDonno [a], Maia Kipman [a], Melissa R. Weiner [b], William D.S. Killgore [a]

[a] Harvard Medical School, McLean Hospital, Department of Psychiatry, 115 Mill Street Belmont, MA 02478, United States
[b] Yale School of Public Health, 60 College St. New Haven, CT 06520, United States

ARTICLE INFO

Article history:
Received 22 October 2012
Received in revised form 4 January 2013
Accepted 15 January 2013
Available online xxxx

Keywords:
Emotional intelligence
Validity
Intelligence quotient
Personality

ABSTRACT

The construct of emotional intelligence (EI) has garnered increased attention in the popular media and scientific literature. Several competing measures of EI have been developed, including self-report and performance-based instruments. The current study replicates and expands on previous research by examining three competing EI measures (Mayer–Salovey–Caruso Emotional Intelligence Test, MSCEIT; Bar-On Emotion Quotient Inventory, EQ-i; and Self-Rated Emotional Intelligence Scale, SREIS) and their relationships with cognitive functioning (Wechsler Abbreviated Scale of Intelligence; WASI), Big Five personality traits (NEO-PI-R) and emotional well-being (Beck Depression Inventory, BDI and Positive and Negative Affect Schedule, PANAS). Results indicated that significant variability in the self-report EI measures was accounted for by personality and emotional well-being measures, whereas the MSCEIT was more strongly associated with IQ. Overall, nearly two-thirds (62%) of the variance in EQ-i scores was accounted for by Big Five personality traits, emotional well-being and full scale IQ; whereas only 14% of the variance in MSCEIT scores was accounted for by these same variables. The present findings raise questions regarding the divergent validity of self-report EI measures from existing personality and emotional well-being measures. The implication of these results and directions for future research are discussed.

1. Introduction

Since the late 1980s, there has been increased interest in the popular media and psychological literature in the concept of *emotional intelligence* (EI; Goleman, 1995; Salovey & Mayer, 1990). Conceptualizations of EI differ widely, as reflected by the broad array of available instruments that have been developed to assess the construct. Existing measures can be broadly categorized as either reflecting *specific ability*, *integrative model*, or *mixed model* conceptualizations of EI (Mayer, Roberts & Barsade, 2008). Specific ability models, as the term implies, highlight the role that a specific ability or set of abilities contribute to EI (e.g., accuracy of emotion perception and emotion regulation). According to integrative models, EI is best defined as an integration of several abilities. The most commonly used integrative measure is the Mayer–Salovey–Caruso Emotional Intelligence Test (MSCEIT; Mayer, Salovey & Caruso, 2002b). The developers of the MSCEIT define EI as the capacity to (1) accurately perceive emotion, (2) use emotions to facilitate thought, (3) understand emotion, and (4) regulate emotions. Accordingly, the test consists of four "branches" (each involving two tasks), which are designed to assess each of the four abovementioned abilities.

In contrast, mixed models adopt a relatively broader conceptualization of EI. For example, Bar-On (2004) defined EI as consisting of "*an array of noncognitive capabilities, competencies, and skills that influence one's ability to succeed in coping with environmental demands and pressures*" ([emphasis in original];

* Corresponding author. Tel.: +1 617 855 4429.
E-mail address: cwebb@mclean.harvard.edu (C.A. Webb).

0160-2896/$ – see front matter © 2013 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.intell.2013.01.004

p. 14). The breadth of the EI definition in mixed models is reflected in the widely used Bar-On Emotional Quotient Inventory (EQ-i; Bar-On, 2002; see http://ei.mhs.com and Bar-On, 2012 for commentary on the recently released EQ-i 2.0), which includes a total of 15 subscales organized under 5 primary scales: 1) *Intrapersonal* (self-regard, emotional self-awareness, assertiveness, independence, and self-actualization), 2) *Interpersonal* (empathy, social responsibility, and interpersonal relationship), 3) *Adaptability* (reality testing, flexibility, and problem solving), 4) *Stress Management* (stress tolerance and impulse control) and 5) *General Mood* (happiness and optimism). Another example of a mixed model conceptualization of EI is reflected in the work of Goleman (1995), who helped popularize the term with his book *Emotional Intelligence*. Goleman's writings suggest that he views EI as a conglomeration of characteristics, including empathy, motivation, persistence, optimism and social skills (Mayer, 1999; Mayer et al., 2002b).

Proponents of integrative models of EI have argued that popular mixed model conceptualizations are overly broad and have become "unmoored" from the core constructs of emotion and intelligence (Mayer, Salovey & Caruso, 2008). For example, Mayer, Caruso, and Salovey (1999) stated that the EQ-i assesses a range of qualities including problem-solving and reality testing that "seem more closely related to ego strength or social competence than to emotional intelligence" (p. 268). Indeed, several studies have reported significant associations between the EQ-i, Big Five personality traits and measures of emotional well-being (e.g., Brackett & Mayer, 2003; Grubb & McDaniel, 2007; Newsome, Day, & Catano, 2000; O'Connor & Little, 2003). The divergent validity of the MSCEIT has also been questioned, with studies reporting significant associations between the latter measure, key personality dimensions, and general intelligence (e.g., Schulte, Ree, & Carretta, 2004; Fiori & Antonakis, 2011).

In summary, debate persists in the field regarding how best to conceptualize and measure EI. Although EI is often discussed in the popular media and psychological literature as if it were a single monolithic construct, dominant EI measures assess a variety of facets (e.g., as reflected by the 15 subscales of the EQ-i and 4 branches of the MSCEIT). The extent to which different EI measures overlap (i.e., convergent validity) and are discriminable (i.e., divergent validity) from theoretically related cognitive (e.g., intelligence quotient [IQ]), personality (e.g., neuroticism and extraversion), and emotional constructs (e.g., affect and mood) is not well understood and is critical for establishing the validity of the EI construct. To our knowledge, no study has concurrently examined the relationship between the most commonly used measures of EI, the Big Five personality traits, emotional well-being, and full scale IQ using one of the Wechsler Intelligence Scales. This is perhaps not surprising given the subject burden and time involved in administering such a large number of measures in one study.

With regard to the existing literature, the majority of previous EI studies have included only one measure of EI (e.g., either an integrative or mixed model measure), rather than comparing several EI measures representing different theoretical models. However, Brackett and Mayer (2003) did include several EI measures in their study (including the EQ-i and MSCEIT), and examined the correlation between EI, Big Five personality traits, and psychological well-being. Interestingly, results indicated that the EQ-i shared substantial variance with personality traits and psychological well-being; whereas the MSCEIT was discriminable from these variables. In addition, and relevant to the divergent validity of EI from traditional cognitive intelligence, Bracket and Mayer found that the MSCEIT, but not the EQ-i, was significantly positively correlated with verbal SAT scores. Although the authors did not assess full scale IQ, verbal SAT scores could be considered a proxy measure of verbal intelligence.

Similar to Brackett and Mayer (2003), previous studies that have examined the association between EI measures and IQ have not used "gold standard" measures of IQ (i.e., full scale Wechsler or Stanford–Binet intelligence scales) but rather have typically used proxy, and less time-consuming, measures of intellectual capacity or restricted their analyses to particular subtests within IQ measures (e.g., see Brackett & Mayer, 2003; Ciarrochi, Chan, & Caputi, 2000; Fiori & Antonakis, 2011; MacCann, Roberts, Matthews, & Zeidner, 2004; O'Connor & Little, 2003; Roberts, Zeidner, & Matthews, 2001; Schulte et al., 2004; Zeidner, Shani-Zinovich, Matthews, & Roberts, 2005). Given the emphasis placed on establishing EI as a type of intelligence, complimenting conventional "cognitive" IQ (Mayer et al., 1999), it is surprising that no study, to our knowledge, has examined the extent to which competing measures of EI correlate with full scale IQ using gold standard measures. It should be noted, however, that Boyatzis, Good, and Massa (2012) recently reported that cognitive intelligence (assessed via the Ravens Advanced Progressive Matrices and Mill Hill Vocabulary test) was not significantly correlated with an informant, multisource assessment of emotional and social intelligence (i.e., the Emotional and Social Competency Inventory; Boyatzis & Goleman, 2007).

The goals of the current study were to examine the convergent validity (i.e., correlation between different EI measures) and divergent validity (i.e., correlation between EI, full scale IQ, Big Five personality traits and emotional well-being) of several commonly used measures of EI. We selected the MSCEIT and EQ-i as they are the most commonly used performance-based and self-report measures of EI, respectively. Differences emerging between the MSCEIT and EQ-i in patterns of associations may be due to differences in the *method of assessment* (performance-based test vs. self-report; i.e., *method variance*) or *content* (i.e., differences in the underlying EI constructs being assessed; i.e., *trait variance*). To control for differences in method of administration, an additional self-report EI measure was included (Self-Rated Emotional Intelligence Scale [SREIS]; Brackett, Rivers, Shiffman, Lerner, & Salovey, 2006), which assesses the same content domains as the MSCEIT but is administered via self-report.

We tested three hypotheses:

1) The two self-report EI measures would be significantly correlated with one another, whereas the performance-based MSCEIT would not be significantly correlated with either self-report EI measure.
2) The EQ-i, but not the MSCEIT, would be significantly associated with personality and emotional well-being measures.
3) The MSCEIT, but not the EQ-i, would be significantly associated with full scale IQ.

2. Method

2.1. Participants

Sixty-five healthy participants (33 males; 32 females) were recruited from the Boston metropolitan area via flyers and internet advertisements. The age of the participants ranged from 18 to 45 with a mean age of 30 (SD = 8.01). The sample was 69.2% Caucasian, 15.4% African-American, 9.2% Asian, 3.1% Other, and 3.1% "more than 1 race." In addition, 4.6% classified themselves as Hispanic. The native language of all participants was English. Participants were screened for evidence of psychopathology and medical conditions by a trained Bachelor's level technician using a structured series of questions. Based on screening, all participants were determined to be free of any history of Axis I psychopathology, excessive substance use, drug or alcohol treatment, or severe medical or neurological conditions. Screening questions were adapted from the Structured Clinical Interview for DSM-IV-TR (SCID-I; First, Spitzer, Gibbon, & Williams, 2001).

2.2. Measures

2.2.1. Emotional intelligence performance-based test

The Mayer–Salovey–Caruso Emotional Intelligence Test (MSCEIT; Mayer et al., 2002b) consists of 141 computer-administered items assessing the perception, use, understanding, and management of emotions. The MSCEIT yields a *Total EI* score and two Area scores, *Experiential EI* and *Strategic EI*. Experiential EI reflects the ability to perceive emotions in oneself, other persons, and different stimuli such as music and art, and to utilize emotional information to facilitate thought. Strategic EI reflects the ability to understand emotions and their evolution in oneself and others, and to manage them in an efficient and effective manner. Mayer, Salovey and Caruso (2002a) reported good reliability values for total MSCEIT scores, including internal consistency (split-half reliability = .91) and test–retest reliability (.86). For additional information on the psychometric properties of the MSCEIT, see Mayer et al. (2002a) and Mayer, Salovey, Caruso, and Sitarenios (2003). The MSCEIT was scored with the recommended "General" scoring option in which scores are based on a normative sample of 5000, rather than the Expert scoring option (i.e., relative to the responses of "emotion experts"; see Mayer et al., 2002a for detailed descriptions of scoring options).

2.2.2. Emotional intelligence self-report measures

Two self-report measures of EI were included in the present study. The Self-Rated Emotional Intelligence Scale (SREIS; Brackett et al., 2006) is a 19-item self-report measure that maps on to the emotional abilities assessed by the MSCEIT. Specifically, similar to the MSCEIT, the SREIS assesses the perception, use, understanding and management of emotions (in both oneself and others). Responses are made on a 5-point Likert scale ranging from 1 ("very inaccurate") to 5 ("very accurate"). In a series of studies, Brackett et al. (2006) reported the following Cronbach's alphas for the SREIS (.84, .77, and .66 for Studies 1, 2, and 3, respectively).

The Bar-On Emotional Quotient Inventory (EQ-i; Bar-On, 2002) is a commonly used 133-item self-report inventory of EI that yields a *Total Emotional Quotient* (EQ) and five composite scores (i.e., *Interpersonal*, *Intrapersonal*, *Adaptability*, *Stress Management*, and *General Mood*). The Interpersonal scale provides a measure of perceived empathy and interpersonal skills, whereas the Intrapersonal scale reflects self-perceived awareness of one's own emotions and self-regard. The Adaptability scale reflects the perceived ability to objectively analyze problematic situations, to solve them and to adapt to changing environments. Stress Management reflects tolerance of and perceived self-control during stressful or demanding situations. The General Mood scale reflects self-reported positive thinking and overall contentedness with personal life. Bar-On (2004) reported that the EQ-i demonstrated good reliability (internal consistency and test–retest reliability). For detailed information on the psychometric properties of the EQ-I, see Bar-On (2004). The EQ-i was scored using the "General Population" norm option (i.e., relative to a North American normative sample of 3831). Responses are made on a 5-point scale (1 = not true of me, 5 = true of me).

2.2.3. Cognitive functioning

The Wechsler Abbreviated Scale of Intelligence (WASI; Pearson Assessment, Inc., San Antonio, TX) was administered to assess cognitive ability. The measure provides scores for Full Scale IQ, Verbal IQ, and Performance IQ. The WASI is one of the most widely used intelligence scales and has reported reliability of .98 for Full Scale IQ, with high test–retest reliability, and correlates .92 with the more comprehensive Wechsler Adult Intelligence Scale-III (WAIS; Pearson Assessment, Inc., San Antonio, TX), the current gold standard in intelligence testing. A trained and experienced bachelor's level research assistant who was blind to the study hypotheses administered and scored the WASI under the supervision of a licensed doctoral level neuropsychologist.

2.2.4. Big Five personality traits

The Revised NEO Personality Inventory (NEO PI-R; Costa & McCrae, 1992) is a 240-item, self-report measure of the Five-Factor Model of personality (i.e., Neuroticism, Extraversion, Openness, Agreeableness, and Conscientiousness). Responses are made on a 5-point Likert scale ranging from *strongly disagree* to *strongly agree*. The NEO PI-R has demonstrated generally adequate reliability: internal consistency = .56–.81; test–retest reliability = .66–.92 (see Costa & McCrae, 1992).

2.2.5. Emotional well-being

Two commonly used measures of emotional well-being were administered to participants. The Positive and Negative Affect Schedule (PANAS; Watson, Clark, & Tellegen, 1988) is a 20-item self-report measure assessing current affective state. The measure consists of 10 items assessing positive affect (e.g., interested and enthusiastic) and 10 items assessing negative affect (e.g., upset and ashamed). Each item is rated on a 5-point scale ranging from 1 ("very slightly or not at all") to 5 ("extremely"). Ratings were averaged to obtain separate subscale scores for positive and negative affect. PANAS scores have demonstrated high test–retest reliability and acceptable convergent validity (Watson et al., 1988). The Beck Depression Inventory (BDI; Beck & Steer, 1987) is a 21-item self-report measure of depressive symptoms, with good psychometric properties (Beck, Steer, & Garbin, 1988).

2.3. Procedure

To minimize participant fatigue, given the relatively large number of performance-based tests and self-report measures administered, testing occurred over two consecutive days. During the first testing session, participants completed demographic forms, consent forms, the MSCEIT, EQ-i, SREIS and PANAS. On the second day of testing, participants completed the WASI, NEO-PI-R and BDI. All assessments were administered according to the standardized instructions provided in the manuals or other published materials. All measures were administered on paper with the exception of the EQ-i and MSCEIT, which were administered online, and the NEO, which was administered via computer. Only one participant was tested at a time. Average total duration of testing was approximately 5 h for Day 1 and 4 h for Day 2. Participants were compensated $200 following the completions of all assessments.

3. Results

3.1. Data analytic strategy

Pearson correlations were used to test the linear associations between EI (MSCEIT, EQ-i and SREIS), IQ (WASI), Big Five personality traits (NEO) and emotional well-being (BDI and PANAS) variables. Means, standard deviations, and correlations for investigated variables are listed in Table 1. Briefly, mean IQ was approximately two-thirds of a standard deviation above the population mean, which is perhaps not surprising given the education level of our sample recruited from the greater Boston area (mean years of schooling = 14.9). EI, personality traits and emotional well-being means were similar to population norms. Three participants did not complete the NEO, WASI or BDI, and one participant did not complete the PANAS. These participants were excluded from the analyses involving these measures.[1] To control for potential confounds associated with socioeconomic status, U.S. Census Bureau data were obtained on the median inflation-adjusted 12-month household income and the percentage of the participant's neighborhood below the poverty line (U.S. Census Bureau, 2010) based on census tract of home address. These census data and categorical data for racial background were used as covariates in a series of partial correlation analyses.[2] Finally, we also conducted a series of hierarchical multiple regression analyses to evaluate the proportion of variance in EI measures accounted for by linear combinations of the predictor variables. Correlations were corrected using the conservative Bonferroni method for multiple comparisons within each separate set of analyses.

3.2. Convergent validity

Using Bonferroni-adjusted alpha levels (.05/3 = .017), scores on the two self-report EI measures (EQ-i and SREIS) were significantly positively correlated with each other ($r = .50$; $p < .001$). Scores on the performance-based MSCEIT were significantly correlated with the SREIS ($r = .32$; $p = .011$) but not with the EQ-i ($r = .11$; $p = .379$).

3.3. Divergent validity with IQ

Using Bonferroni-adjusted p-values (.05/9 = .006), the MSCEIT was significantly correlated with Full Scale IQ ($r = .52$; $p < .001$), Verbal IQ ($r = .52$; $p < .001$), and Performance IQ ($r = 43$; $p < .001$). The SREIS was significantly correlated with Verbal IQ ($r = .37$; $p = .003$), but not with Performance IQ ($r = .17$; $p = .180$) or Full Scale IQ ($r = .30$; $p = .017$). As evident in Table 1, the EQ-i did not correlate with Full Scale IQ ($r = .22$; $p = .085$), Performance IQ ($r = .24$; $p = .060$), or Verbal IQ ($r = .17$; $p = .194$).

Of note, the MSCEIT remained significantly associated with all three IQ variables in partial correlation analyses controlling for socioeconomic and demographic variables including age, neighborhood median household income, percentage of the neighborhood below the poverty line, and ethnic status (all $rs > .45$ and $ps < .006$). However, the SREIS was no longer significantly associated with Verbal IQ ($r = .28$; $p = .049$).

3.4. Divergent validity with Big Five personality traits

Using Bonferroni-adjusted alpha levels (.05/15 = .003), the MSCEIT was not significantly correlated with any of the Big Five traits (Neuroticism $r = -.17$, $p = .198$; Extraversion $r = -.02$, $p = .890$; Agreeableness $r = .11$, $p = .404$; Conscientiousness $r = -.14$, $p = .265$; and Openness $r = .23$, $p = .068$).

In contrast, significant associations did emerge between the two self-report EI measures and the Big Five. Specifically, the SREIS was significantly correlated with Extraversion ($r = .41$; $p = .001$) and Openness ($r = .45$; $p < .001$). The SREIS, however, was not significantly correlated with either Neuroticism ($r = -.28$; $p = .030$), Agreeableness ($r = .20$; $p = .121$) or Conscientiousness ($r = .20$; $p = .113$). The EQ-i was significantly correlated with three of the Big Five factors (Neuroticism $r = -.60$, $p < .001$; Extraversion $r = .46$, $p < .001$; Conscientiousness $r = .49$, $p < .001$; but not with Openness $r = .32$, $p = .011$ or Agreeableness $r = .20$, $p = .121$).

3.5. Divergent validity with emotional well-being

Next, and while using Bonferroni-adjusted p-values (.05/9 = .006), we examined the association between EI, negative and positive affect (PANAS — NA/PA) and depressive symptoms (BDI). The MSCEIT was not significantly associated with scores on the BDI ($r = -.10$; $p = .433$), PANAS — NA ($r = -.17$; $p = .193$) or PANAS — PA ($r = -.19$; $p = .132$).

[1] Three outliers were identified and deleted. Specifically, one outlier for the BDI ($z = 4.91$) and two outliers for the PANAS — Negative Affect subscale ($z = 4.33$; $z = 3.40$) were identified. These datapoints were deleted.

[2] There were no significant gender differences in mean EI, IQ, Big Five personality traits, BDI or PANAS scores. In addition, given some evidence that IQ and EI increase with age (e.g., Bar-On, 2004; Mayer et al., 2002a), we tested the correlation between age and scores on the WASI, MSCEIT, EQ-i and SREIS. All correlations were non-significant with the exception of a significant *negative* correlation between age and SREIS scores ($r = -.39$; $p = .001$). Given that the SREIS is a self-report measure of EI, such a negative association may reflect the fact that younger participants are more likely to *perceive* themselves as having higher EI than older participants (whether or not their actual EI is higher than older participants). Of course, this one significant correlation must be interpreted in the context of non-significant correlations between age and the most commonly used self-report (EQ-i) and performance-based (MSCEIT) EI measures.

Table 1
Means, standard deviations and correlations for investigated variables.

Variable	M	SD	2	3	4	5	6	7	8	9	10	11	12	13	14
1. MSCEIT	103.06	12.09	.11	.32*	.52**	.52**	.43**	−.17	−.02	.23	−.14	.11	−.10	−.19	−.17
2.EQ-i	101.42	13.63	—	.50**	.22	.17	.24	−.60**	.46**	.32*	.49**	.20	−.46**	.32**	−.26*
3. SREIS	3.85	0.42		—	.30*	.37**	.17	−.28*	.41**	.45**	.20	.20	−.54**	.13	−.08
4.IQ-Full	111.10	16.08			—	.92**	.91**	−.27*	.12	.40**	−.11	.28*	−.35**	−.19	−.05
5.IQ-Verbal	110.40	15.76				—	.69**	−.21	.07	.37**	−.14	.23	−.38**	−.26**	.02
6.IQ-Perf.	108.85	15.43					—	−.30*	.15	.36**	−.06	.28*	−.25*	−.10	−.09
7. NEO-N	50.81	11.21						—	−.25	−.20	−.11	−.11	.48**	−.04	.19
8. NEO-E	54.55	11.70							—	.10	.04	.15	−.24	.25	.06
9. NEO-O	55.16	10.40								—	.13	.35**	−.32*	.00	.00
10. NEO-C	50.10	12.21									—	−.04	−.26*	.35**	−.22
11. NEO-A	47.53	11.02										—	−.21	.06	−.07
12. BDI	3.61	4.44											—	−.21	.24
13. PANAS − PA	29.03	7.46												—	−.17
14. PANAS − NA	11.65	2.33													—

Note: MSCEIT = Mayer−Salovey−Caruso Emotional Intelligence Test; EQ-i = Bar-On Emotional Quotient Inventory; SREIS = Self-Rated Emotional Intelligence Scale; IQ-Full/Verbal/Performance = Wechsler Abbreviated Scale of Intelligence — Full-Scale/Verbal IQ/Performance IQ; NEO-N/E/O/C/A = The Revised NEO Personality Inventory — Neuroticism, Extraversion, Openness, Conscientiousness, and Agreeableness; BDI = Beck Depression Inventory; PANAS = Positive and Negative Affect Schedule.
* $p<.05$.
** $p<.01$.

In contrast, a significant negative correlation emerged between the SREIS and BDI ($r=-.54$; $p<.001$). However, there was no significant association between the SREIS and either the PANAS − NA ($r=-.08$; $p=.533$) or PANAS − PA ($r=.13$; $p=.291$). Similarly, the EQ-i was significantly negatively correlated with the BDI ($r=-.46$; $p<.001$), but not with the PANAS − NA ($r=-.26$; $p=.044$) or PANAS − PA ($r=.32$; $p=.010$).

3.6. Multiple regressions including all predictors

Given the associations between IQ, Big Five traits, and emotional well-being measures (see Table 1), multiple regression analyses were conducted to test which of these variables would remain significantly associated with EI when competing variables are included as covariates (standardized betas [βs] and associated p values are reported below). In addition, such a comprehensive model allowed us to estimate the percentage of variance (adjusted R^2) associated with each EI measure that is accounted for by the combination of independent variables (IVs). See Fig. 1 for a graphical representation of multiple regression results.

First, a comprehensive model was tested in which full scale IQ, each of the Big Five traits, and the three emotional well-being variables were included as IVs, and the MSCEIT was the dependent variable (DV). A nonsignificant trend emerged for the overall model (F (9, 48) = 2.05, $p=.057$), with an adjusted $R^2=.14$. Only full scale IQ remained significantly associated with the MSCEIT when all other independent variables were controlled ($\beta=0.45$, $p=.006$; all other ps > .37).

The same comprehensive model, including all study IVs, was examined with the SREIS as the DV. In this case, the overall model was significant (F (9, 48) = 4.51, $p<.001$), with an

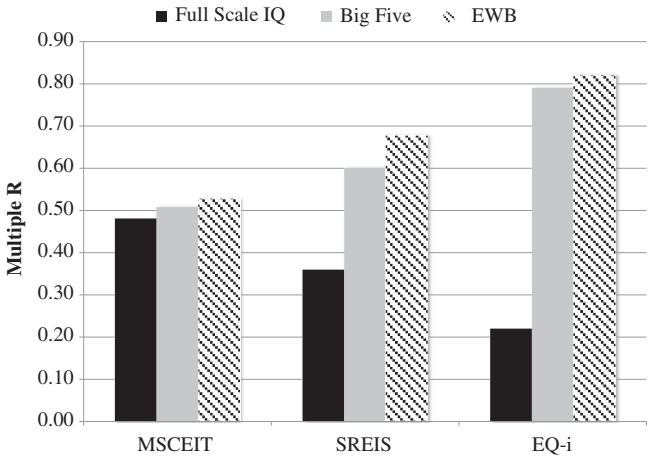


Fig. 1. Multiple *R*s for Full Scale IQ, Big Five traits and emotional well-being (EWB) scales regressed on total EI scores for the MSCEIT, EQ-i, and SREIS. Specifically, three hierarchical multiple regressions were conducted (one for each EI measure). For each regression, independent variables were entered in three blocks (Full Scale IQ in Block 1, Big Five traits in Block 2, and emotional well-being scales in Block 3). The sample size for each of these three regressions was 58. With regards to collinearity diagnostics, Tolerance values ranged between .62 and .83, and thus did not indicate any concerning multicollinearity (Field, 2009; Menard, 1995).

adjusted $R^2 = .36$. The Big Five traits of Extraversion ($\beta = 0.31$, $p = .012$) and Openness ($\beta = 0.30$, $p = .030$) were positively associated with SREIS scores. In addition, scores on the BDI were negatively associated with the SREIS ($\beta = -0.39$, $p = .006$). All other $ps > .38$.

Finally, the above comprehensive model was tested with the EQ-i as the DV. The overall model was significant ($F(9, 48) = 11.25$, $p < .001$), with an adjusted $R^2 = .62$. (The adjusted R^2 remained .62 even when full scale IQ was excluded from the model.) Three of the Big Five traits were significantly associated with EQ-i scores (Neuroticism $\beta = -0.32$, $p = .002$; Extraversion $\beta = 0.34$, $p < .001$; and Conscientiousness $\beta = 0.32$, $p < .001$). Openness was associated with the EQ-i at the level of a nonsignificant trend ($\beta = 0.21$, $p = .053$). In addition, scores on the PANAS — PA were positively associated with the EQ-i ($\beta = 0.22$, $p = .021$). All other $ps > .34$.

4. Discussion

Although there is general agreement that the ultimate relevance of emotional intelligence (EI) lies in its ability to predict important life outcomes (e.g., quality of interpersonal relationships, academic or occupational success), debate persists in how best to operationalize (e.g., integrative versus mixed models) and measure EI (e.g., self-report versus performance-based instruments). Different conceptualizations of EI are reflected in the broad array of available instruments that have been developed to assess the construct. The current study investigated the convergent and divergent validity of several competing measures of EI (MSCEIT, EQ-i, and SREIS). Consistent with our hypotheses, and paralleling the findings of Brackett and Mayer (2003), we found that the performance-based MSCEIT was discriminable from the personality and emotional well-being (EWB) variables we examined, whereas the two self-report measures of EI (EQ-i and SREIS) shared significant variance with these variables. This was particularly true for the EQ-i. Indeed, whereas the MSCEIT was not significantly associated with any of the personality or EWB variables examined, the EQ-i was significantly correlated with all but one of these variables at conventional statistical significance levels ($p < .05$; i.e., 4 of the Big Five personality traits and all 3 of the EWB variables; see Table 1). In addition to the findings of Bracket and Mayer, several previous studies have also reported significant associations between the EQ-i, Big Five personality traits, and measures of emotional/psychological well-being (e.g., Grubb & McDaniel, 2007; Newsome et al., 2000; O'Connor & Little, 2003). Overall, and as discussed in more detail below, the current findings raise concerns regarding the extent to which the EQ-i is discriminable from existing personality and EWB constructs.

As noted above, the EQ-i was designed to assess a broad "*array of noncognitive capabilities, competencies and skills*" ([emphasis in original]; Bar-On, 2004, p. 14), including items measuring constructs that seem to overlap substantially with EWB and Big Five personality traits (e.g., scales assessing optimism, happiness, stress tolerance, self-regard, self-actualization, and impulse control). Thus, given the items comprising the EQ-i, it is perhaps not surprising that the measure was found to be significantly associated with the EWB and personality measures included in the current study.

In addition to the overlap in semantic content between the EQ-i and emotion/personality measures, similarities in method of assessment may help account for the patterns of associations we observed. More specifically, given that the EQ-i, Big Five personality traits, and EWB variables were each assessed via self-report, significant correlations between these variables may have been due in part to *shared method variance* (Kazdin, 2003). It should be noted, however, that a third EI measure (SREIS) was included in the current study, which was also administered via self-report but was designed to assess the same content domains as the MSCEIT. The fact that the SREIS exhibited relatively weaker associations with EWB and personality variables than did the EQ-i suggests that the particularly strong associations between the latter measure and EWB/personality variables may be due at least in part to overlap in actual content (i.e., *trait variance*) rather than due entirely to shared method variance.

Furthermore, the difference in patterns of correlations between the performance-based MSCEIT and self-report measures may have been due in part to the influence of mood/affect on *perception* of EI. For example, those subjects with relatively higher levels of depressed mood may be more likely to *perceive* themselves as possessing low levels of EI, regardless of their "actual" EI (reflected in a significant negative association between BDI scores and both SREIS and EQ-i total scores). In contrast, given that the MSCEIT is a performance-based test rather than a self-report questionnaire, it may be less susceptible to perceptual biases associated with emotional state (as reflected in a lack of association between EWB variables and MSCEIT scores).

It is important to note that significant correlations with personality and EWB variables do not necessarily impugn the validity of the EQ-i. Indeed, as noted above, the scale was explicitly designed to contain subscales assessing a variety of facets, including domains overlapping with EWB and personality dimensions (Bar-On, 2002, 2004). In other words, the domains assessed in the EQ-i ultimately reflect the perspective of the test developer regarding what constitutes EI (Bar-On, 2006). On the other hand, the current findings indicate that nearly *two-thirds* (62%) of the variance in EQ-i scores was accounted for by Big Five personality traits and EWB; whereas only 14% of the variance in MSCEIT scores was accounted for when all variables were included in the model. These findings raise the important question: How much additional information does the EQ-i provide above and beyond existing personality and EWB measures? It will be important for future studies of EI to include Big Five personality traits and EWB measures as covariates in their analyses to reduce the risk of third variable confounds (e.g., a significant association between EI and important life outcomes may in fact be a spurious correlation accounted for by Big Five personality traits and/or EWB).

In contrast to the findings regarding personality and EWB, and consistent with our hypothesis, IQ was more strongly associated with the MSCEIT than either of the two self-report EI measures (although a significant correlation did emerge between the SREIS and verbal IQ). In addition to including several competing measures of EI, one of the strengths of the current study was the assessment of full scale IQ using a reliable and well-validated instrument (i.e., WASI). Previous studies have typically used proxy, and less time-consuming,

measures of IQ or restricted their analyses to particular subtests of IQ measures (e.g., Brackett & Mayer, 2003; Ciarrochi et al., 2000; MacCann et al., 2004; O'Connor & Little, 2003; Roberts et al., 2001; Schulte et al., 2004; Zeidner et al., 2005). In light of the current pattern of findings, it is interesting to note that the developers of the MSCEIT emphasized the importance of establishing EI as a type of intelligence, complementing traditional IQ (Mayer et al., 1999; Mayer & Salovey, 1993). In statistical terms, the authors argued that a valid measure of EI should correlate moderately with, but remain discriminable from, IQ. Correlations between the MSCEIT and IQ scales were in the "moderate" to "large" range in the current study (Cohen, 1992). Interestingly, the EI measure with the second strongest association with IQ was the SREIS (same content as MSCEIT but different assessment method), followed by the EQ-i (both different content and different method of assessment than the MSCEIT). These findings suggest that it will also be important to control for IQ in future EI studies, particularly when performance-based measures of EI are being employed. Moreover, given the distinction intelligence theorists have made between fluid (*Gf*) and crystallized intelligence (*Gc*), fruitful findings may also emerge from future research examining the relationship between EI and *Gf* versus *Gc*. Previous findings have suggested a relationship between the MSCEIT and both *Gf* (e.g., Di Fabio & Palazzeschi, 2009; Fiori & Antonakis, 2012) and *Gc* (Mayer, Roberts, et al., 2008). As well, within our own dataset, we found significant correlations between the MSCEIT and variables arguably tapping *Gf* (MSCEIT–WASI [Performance IQ] $r = .43$) and *Gc* (MSCEIT–WASI [vocabulary subtest] $r = .542$).

Finally, with regard to convergent validity, it is interesting to note that the two self-report measures of EI (i.e., EQ-i and SREIS) – which cover different content – were more highly correlated than the MSCEIT and SREIS which were designed to cover the same content, but used different methods of assessment (i.e., performance-based versus self-report, respectively). There are a number of different interpretations of these results, but the latter pattern of findings may reflect the effect of shared method variance on influencing the strengths of correlations between EI measures. Furthermore, to the extent that the MSCEIT does accurately assess EI, these findings may reflect the fact that, on average, an individual's report of their own EI abilities and actual EI performance do not correlate highly. Indeed, self-report measures are inherently limited by the fact that they rely on an individual's ability to accurately assess and report on the construct being assessed (in this case, EI). Similar criticisms have also been raised of the validity of self-report measures of IQ (Paulhus, Lysy, & Yik, 1998). Worthwhile findings may emerge from research utilizing other approaches to assessing EI, including multisource ("360°") assessments, videotapes of simulations or behavioral coding of taped interviews (Boyatzis, 2009; Boyatzis et al., 2012).

4.1. Limitations

Several limitations of the current study should be noted. First, our sample size was small, limiting statistical power. Nevertheless, we found a number of significant and intriguing relationships in line with our hypotheses, despite the fact that the especially conservative Bonferroni method was employed to adjust for multiple comparisons (Perneger, 1998; Rothman, 1990). Second, the current study was cross-sectional and not a prospective, longitudinal investigation, which prevented us from drawing inferences regarding the direction of associations (e.g., between emotional well-being and EI), and predicting longer-term life outcomes from EI scores (e.g., changes in interpersonal relationships, academic or occupational success). Third, we used the abbreviated WASI rather than the full WAIS to assess IQ. Finally, we should also reiterate that the SES data we obtained was from U.S. census tract statistics (U.S. Census Bureau, 2010) rather than a measure of each participant's individual SES status.

4.2. Future directions

More studies are needed which directly compare the psychometric characteristics of competing EI measures, including their convergent and divergent validity relative to existing measures of personality traits, emotion constructs and cognitive functioning. Ultimately, as noted above, it will be critical for studies to compare the incremental predictive validity of competing EI measures in predicting relevant life outcomes, after controlling for relevant personality variables and IQ. The results of such research may help inform the development of improved EI measures. In addition, the application of EI research to clinical populations may yield fruitful findings. For example, although effective psychosocial interventions have been developed and tested for clinical depression, the "active ingredients" of these treatments and precise mechanisms of symptom change remain unclear. Perhaps improvements in EI, or particular facets of EI (e.g., emotion management), in part mediate the therapeutic improvement experienced by clinically depressed patients in psychotherapy (e.g., in cognitive behavioral therapy which directly targets emotion regulation skills).

References

Bar-On, R. (2002). *Bar-On Emotional Quotient Inventory: User's manual.* Toronto: Multi-Health Systems.

Bar-On, R. (2004). *Bar-On Emotional Quotient Inventory: A measure of emotional intelligence — Technical manual.* North Tonawanda, NY: Multi-Health Systems.

Bar-On, R. (2006). The Bar-On model of emotional–social intelligence (ESI). *Psicothema*, *18*, 13–25 (Suppl.).

Bar-On, R. (2012). The impact of emotional intelligence on health and wellbeing. In A. Di Fabio (Ed.), *Emotional intelligence — New perspectives and applications* (pp. 78–92). : InTech.

Beck, A. T., & Steer, R. A. (1987). *Beck Depression Inventory manual.* San Antonio, TX: Harcourt Brace.

Beck, A. T., Steer, R. A., & Garbin, M. G. (1988). Psychometric properties of the Beck Depression Inventory: Twenty-five years of evaluation. *Clinical Psychology Review*, *8*, 77–100.

Boyatzis, R. E. (2009). Competencies as a behavioral approach to emotional intelligence. *The Journal of Management Development*, *28*, 749–770.

Boyatzis, R. E., & Goleman, D. (2007). *Emotional Competency Inventory (now the Emotional and Social Competency Inventory).* Boston, MA: Hay Group.

Boyatzis, R. E., Good, D., & Massa, R. (2012). Emotional, social, and cognitive intelligence and personality as predictors of sales leadership. *Journal of Leadership & Organizational Studies*, *19*, 191–201.

Brackett, M. A., & Mayer, J. D. (2003). Convergent, discriminant, and incremental validity of competing measures of emotional intelligence. *Personality & Social Psychology Bulletin*, *29*(9), 1147–1158. http://dx.doi.org/10.1177/0146167203254596.

Brackett, M. A., Rivers, S. E., Shiffman, S., Lerner, N., & Salovey, P. (2006). Relating emotional abilities to social functioning: A comparison of self-report and performance measures of emotional intelligence. *Journal of Personality and Social Psychology*, *91*(4), 780–795. http://dx.doi.org/10.1037/0022-3514.91.4.780.

Ciarrochi, J. V., Chan, A. Y. C., & Caputi, P. (2000). A critical evaluation of the emotional intelligence construct. *Personality and Individual Differences*, *28*, 539–561.

Cohen, J. (1992). A power primer. *Psychological Bulletin*, *112*, 155–159.

Costa, P. T., Jr., & McCrae, R. R. (1992). *Revised NEO personality inventory manual.* Odessa, FL: Psychological Assessment Resources.

Di Fabio, A., & Palazzeschi, L. (2009). An in-depth look at scholastic success: Fluid intelligence, personality traits or emotional intelligence? *Personality and Individual Differences*, *46*(5), 581–585.

Field, A. (2009). *Discovering statistics using SPSS* (3rd ed.). Thousand Oaks, CA: Sage Publications, Inc.

Fiori, M., & Antonakis, J. (2011). The ability model of emotional intelligence: Searching for valid measures. *Personality and Individual Differences*, *50*, 329–334.

Fiori, M., & Antonakis, J. (2012). Selective attention to emotional stimuli: What IQ and openness do, and emotional intelligence does not. *Intelligence*, *40*(3), 245–254.

First, M., Spitzer, R., Gibbon, M., & Williams, J. (2001). *Structured Clinical Interview for DSM-IV-TR — Axis I Disorders, Research Version, Patient Edition with Psychotic Screen (SCID-I/P W/PSY SCREEN).* Biometrics Research, New York State Psychiatric Institute.

Goleman, D. (1995). *Emotional intelligence.* New York: Bantam.

Grubb, W. L., & McDaniel, M. A. (2007). The fakability of Bar-On's Emotional Quotient Inventory short form: Catch me if you can. *Human Performance*, *20*, 43–59.

Kazdin, A. E. (2003). *Research design in clinical psychology* (4th ed.). Needham Heights, MA: Allyn & Bacon.

MacCann, C., Roberts, R. D., Matthews, G., & Zeidner, M. (2004). Consensus scoring and empirical option weighting of performance-based Emotional Intelligence (EI) tests. *Personality and Individual Differences*, *36*, 645–662.

Mayer, J. D. (1999). Emotional intelligence: Popular or scientific psychology? *APA monitor*, *30*, 50.

Mayer, J. D., Caruso, D. R., & Salovey, P. (1999). Emotional intelligence meets traditional standards for an intelligence. *Intelligence*, *27*, 267–298.

Mayer, J. D., Roberts, R. D., & Barsade, S. G. (2008). Human abilities: Emotional intelligence. *Annual Review of Psychology*, *59*(1), 507–536. http://dx.doi.org/10.1146/annurev.psych.59.103006.093646.

Mayer, J. D., & Salovey, P. (1993). The intelligence of emotional intelligence. *Intelligence*, *17*, 433–442.

Mayer, J. D., Salovey, P., & Caruso, D. (2002a). *MSCEIT technical manual.* Toronto, Ontario, Canada: Multi-Health Systems.

Mayer, J. D., Salovey, P., & Caruso, D. (2002b). *The Mayer–Salovey–Caruso Emotional Intelligence Test (MSCEIT), Version 2.0.* Toronto, Ontario, Canada: Multi-Health Systems.

Mayer, J. D., Salovey, P., & Caruso, D. R. (2008). Emotional intelligence: New ability or eclectic traits? *American Psychologist*, *63*, 503–517.

Mayer, J. D., Salovey, P., Caruso, D., & Sitarenios, G. (2003). Measuring emotional intelligence with the MSCEIT V2.0. *Emotion*, *3*, 97–105.

Menard, S. (1995). *Applied logistic regression analysis. Sage University paper series on quantitative applications in the social sciences*, *07–106*, Thousand Oaks, CA: Sage.

Newsome, S., Day, A. L., & Catano, V. M. (2000). Assessing the predictive validity of emotional intelligence. *Personality and Individual Differences*, *29*, 1005–1016.

O'Connor, R. M., & Little, I. S. (2003). Revisiting the predictive validity of emotional intelligence: Self-report versus ability-based measures. *Personality and Individual Differences*, *35*(8), 1893–1902. http://dx.doi.org/10.1016/s0191-8869(03)00038-2.

Paulhus, D. L., Lysy, D. C., & Yik, M. S. M. (1998). Self-report measures of intelligence: Are they useful as proxy IQ tests. *Journal of Personality*, *66*(4), 525–554.

Perneger, T. V. (1998). What's wrong with Bonferroni adjustments. *British Medical Journal*, *316*(7139), 1236–1238.

Roberts, R. D., Zeidner, M., & Matthews, G. (2001). Does emotional intelligence meet traditional standards for an intelligence? Some data and conclusions. *Emotion*, *1*, 196–231.

Rothman, K. J. (1990). No adjustments are needed for multiple comparisons. *Epidemiology*, *1*(1), 43–46.

Salovey, P., & Mayer, J. D. (1990). Emotional intelligence. *Imagination, Cognition, Personality*, *9*, 185–211.

Schulte, M. J., Ree, M. J., & Carretta, T. R. (2004). Emotional intelligence: Not much more than g and personality. *Personality and Individual Differences*, *37*, 1059–1068.

U.S. Census Bureau (2010). Selected social characteristics in the United States: 2006–2010. *2006–2010 American Community Survey* (Retrieved June 20, 2012, http://factfinder2.census.gov)

Watson, D., Clark, L. A., & Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect: The PANAS scales. *Journal of Personality and Social Psychology*, *54*, 1063–1070.

Zeidner, M., Shani-Zinovich, I., Matthews, G., & Roberts, R. D. (2005). Assessing emotional intelligence in gifted and non-gifted high school students: Outcomes depend on the measure. *Intelligence*, *33*, 369–391.

NeuroImage 71 (2013) 216–223

Contents lists available at SciVerse ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

Daytime sleepiness affects prefrontal regulation of food intake ☆

William D.S. Killgore *, Zachary J. Schwab, Mareen Weber, Maia Kipman, Sophie R. DelDonno, Melissa R. Weiner, Scott L. Rauch

Social, Cognitive and Affective Neuroscience Lab, McLean Hospital, Harvard Medical School, USA

ARTICLE INFO

Article history:
Accepted 8 January 2013
Available online 24 January 2013

Keywords:
Sleep
Sleepiness
Food
Appetite
Sex differences
Prefrontal cortex
fMRI
Neuroimaging

ABSTRACT

The recent epidemic of obesity corresponds closely with the decline in the average number of hours of sleep obtained nightly. While growing research suggests that sleep loss may affect hormonal and other physiological systems related to food intake, no studies have yet explored the role that sleepiness may play in reducing prefrontal inhibitory control over food intake. Because evidence suggests that women may be more prone to obesity and eating disorders, as well as more likely to suffer from sleep problems, we examined the relation between general daytime sleepiness, brain responses to food stimuli, and self-reported overeating separately for men and women. Thirty-eight healthy adults (16 women; 22 men) aged 18 to 45 underwent functional magnetic resonance imaging (fMRI) while viewing pictures of high- and low-calorie foods. Subjects completed the Epworth Sleepiness Scale (ESS) and provided a rating to the query "how often do you eat more than you intend to." Contrast images comparing brain activation derived from the high- versus low-calorie conditions were correlated voxel-wise with scores from the ESS in a second-level regression model, the output of which was used to predict self-reported overeating. As hypothesized, daytime sleepiness correlated with reduced activation in the ventromedial prefrontal cortex during perception of high- versus low-calorie food images. Moreover, activation within this cluster predicted overeating, but only for women. Findings suggest that normal fluctuations in sleepiness may be sufficient to affect brain regions important for regulating food intake, but that these effects may differ between men and women.

Introduction

Over the past several decades there has been an alarming increase in the rate of excessive weight gain in Western societies (Flegal et al., 2002), with over one in three adults in the United States now meeting criteria for obesity (Ogden et al., 2012). While there are many factors that have arguably contributed to this trend, it is hard to ignore the fact that obesity rates have closely paralleled the decline in average nightly sleep during the latter portion of the 20th century. Evidence suggests that during the 1960s, Americans were sleeping between 8.0 and 8.9 h per night (Kripke et al., 1979). By the mid 1990s, average sleep had declined to about 7.0 h (Gallup Organization, 1995), and recent data from 2005 suggest that most Americans are now sleeping less than 7 h per night (National Sleep Foundation, 2005). In fact, a 2012 report by the Center for Disease Control and Prevention (CDC) found that one in three workers now report that they routinely sleep six or fewer hours nightly (Center for Disease Control and Prevention, 2012). Shorter sleep duration is related to a variety of health problems including obesity (Patel et al., 2008). Moreover, short sleep duration earlier in life is related to increased risk of weight gain later in life (Gangwisch et al., 2005; Hasler et al., 2004; Patel, 2009). The relation between sleep and weight gain is poorly understood, but may prove crucial to stopping or even reversing the current trends.

Notably, the epidemic of obesity has particularly affected women. Epidemiological studies suggest that for the past few decades, women have shown significantly higher rates of obesity compared to men (Ogden et al., 2012), and extreme levels of obesity (i.e., Body Mass Index > 40) are more than twice as prevalent among women than men (Ogden et al., 2006). It has also long been known that women tend to be at much greater risk for developing a number of different eating related problems and clinical eating disorders relative to men (Lewinsohn et al., 2002; Striegel-Moore and Bulik, 2007; Striegel-Moore et al., 2009). While the reasons for the gender differences in eating disorders are not fully understood, some evidence suggests that there may be some cognitive and behavioral differences in responses to food, with women more frequently reporting a greater perception of loss of control over the amount of food consumed during meals (Striegel-Moore et al., 2009). Functional neuroimaging studies have also suggested that there may be sex differences in responses of key appetite regions to images of food (Killgore and Yurgelun-Todd, 2010). Interestingly, the reported sex differences in food consumption

☆ Funding: This research was supported by a USAMRAA grant (W81XWH-09-1-0730).
* Corresponding author at: Social, Cognitive, and Affective Neuroscience Lab, McLean Hospital, Harvard Medical School, 115 Mill Street, Belmont, MA 02478, USA. Fax: +1 617 855 2770.
E-mail address: killgore@mclean.harvard.edu (W.D.S. Killgore).

1053-8119/$ – see front matter © 2013 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.neuroimage.2013.01.018

also appear to be mirrored in the frequency of some sleep-related complaints and disorders. For instance, a recent meta-analysis of studies of insomnia showed that women were over 1.4 times more likely to suffer from insomnia compared to men (Zhang and Wing, 2006). Although sleep apnea is more common among middle to older age men (O'Connor et al., 2000), general non-respiratory sleep complaints such as poor sleep quality, longer sleep onset latency, and difficulty with sleep maintenance tend to be more common among women in the same age range (Middelkoop et al., 1996). A recent poll by the National Sleep Foundation reported that 67% of women experience sleep problems at least a few nights each week and 46% report that they suffer from sleep problems every night (National Sleep Foundation, 2007). Thus, over the past few decades, sleep duration has declined while obesity has increased, and these problems appear to be particularly common among women.

Most studies linking insufficient sleep to excess food consumption and weight gain have emphasized the effects of sleep loss on physiological variables such as reduced energy expenditure and alterations in the hormones leptin and ghrelin, which are key regulators of appetite (Knutson et al., 2007; Patel and Hu, 2008). However, lack of sleep can affect other systems that play a role in food intake as well. For instance, sleep loss is associated with altered functional activity within a number of brain regions. Of particular relevance to food consumption is the prefrontal cortex, particularly the ventromedial prefrontal cortex (vmPFC), a complex brain region that is particularly important for evaluating the reward value of objects (Paulus and Frank, 2003), regulating emotional responses (Hariri et al., 2003), and controlling behavior (Blasi et al., 2006; Ridderinkhof et al., 2004). Sleep loss is associated with a number of changes in the vmPFC, including reduced glucose metabolism (Thomas et al., 2000; Wu et al., 2006), altered functional responses during risky decision-making (Venkatraman et al., 2007) and judgments of economic value (Libedinsky et al., 2011; Venkatraman et al., 2011), as well as reduced functional connectivity with other brain regions important for self-referential and emotional processing (De Havas et al., 2012; Killgore et al., 2012c; Samann et al., 2010; Yoo et al., 2007). When sleep is lacking, these prefrontal changes appear to contribute to deficits in decision-making and inhibitory control (Drummond et al., 2006; Harrison and Horne, 2000; Killgore, 2010). Interestingly, recent data suggest that general daytime sleepiness is associated with reduced gray matter volume within the vmPFC (Killgore et al., 2012b). Some of these same sleep-sensitive prefrontal systems have previously been shown to be critical in responding to the caloric content of visually presented food stimuli (Killgore and Yurgelun-Todd, 2005b; Killgore et al., 2003) and may even relate to greater body mass index (BMI) (Killgore and Yurgelun-Todd, 2005a). Thus, evidence suggests that insufficient sleep alters functioning in key brain regions that are particularly responsive to the caloric content of food and which are important for regulating and inhibiting behavior.

The goal of the present study was to examine the relation between self-reported general daytime sleepiness and prefrontal cortex responses to the calorie content of food images. Based on the neuroimaging and behavioral literature outlined above, we hypothesized that greater general daytime sleepiness would be associated with reduced functional responsiveness of the vmPFC to high- versus low-calorie food images, and that the magnitude of responsiveness within this inhibitory region would predict self-reported problems with overeating. Furthermore, given the sex differences in the current rates of obesity, eating disorders, and sleep complaints, we also hypothesized that the relationships would be stronger in women than in men.

Methods

Participants

Thirty-eight healthy right-handed adults, ranging in age from 18 to 45 years (16 women, 22 men), were recruited via flyers and internet advertisements posted around Boston, MA, and the surrounding areas. Participants were thoroughly screened by a trained research technician during a semi-structured interview. Based on this screening, enrolled participants were deemed to be free of any evidence or history of severe medical conditions, head injury, loss of consciousness >30 min, brain tumors, seizures, neurologic conditions, symptoms consistent with Axis I psychopathology, or drug or alcohol treatment. Additionally, potential participants were excluded for current or recent use of any psychoactive medications or illicit substances, or excessive alcohol intake. Table 1 provides basic demographic information for the women and men separately. Body mass index (BMI) ranged from normal (19.80) to moderately obese (34.78) for the sample as a whole (M = 24.60, SD = 3.75), but this did not differ between women and men (see Table 1). Each participant completed detailed logs of all food consumed on the day of the scan. Two independent raters used the food logs to calculate each participant's calorie consumption during the hours preceding the scan via a primary web-based resource for determining calorie content from foods (http://ndb.nal.usda.gov), and relied on a secondary resource when a definitive answer could not be obtained from the first (http://caloriecount.about.com). Inter-rater reliability in calorie scoring was extremely high (ICC = 0.97, CI = 0.95–0.98), and the independent ratings were averaged for each participant to obtain a final estimate of total calorie consumption. On the whole, participants consumed an average of 327.8 calories (SD = 243.6) during the hours leading up to the scan, with no significant difference between women and men in calorie intake (see Table 1). Overall, typical caffeine use was modest, ranging from 0 to 444 mg per day (M = 104.08, SD = 117.65), and did not differ between women and men. Similarly, caffeine use on the day of the scan was not significantly different for the women and men. Participants reported generally normal amounts of weeknight (M = 7.36, SD = 0.88 h) and weekend sleep (M = 7.71, SD = 1.32 h), as well as normal amounts of sleep the night before the scan (M = 7.04,

Table 1
Demographic and performance variable information for participants.

	Men (n = 22)		Women (n = 16)			
	M	SD	M	SD	t (df = 36)	sig.
Age (years)	31.50	9.30	28.25	7.48	1.19	ns
BMI (weight [kg]/height [m]^2)	24.24	3.60	25.08	4.01	−0.68	ns
Pre-scan calories consumed	358.8	236.7	285.1	254.1	0.92	ns
Typical caffeine use (mg/day)	101.94	127.48	107.02	106.64	−0.13	ns
Study day caffeine use (mg)	73.96	122.17	88.91	106.27	−0.39	ns
Weeknight sleep (h)	7.36	0.94	7.36	0.81	0.02	ns
Weekend sleep (h)	7.82	1.31	7.56	1.38	0.58	ns
Last night sleep (h)	6.91	0.97	7.22	0.93	−0.99	ns
ESS	5.77	3.74	5.31	3.18	0.40	ns
Current hunger (1–7)	4.64	1.33	5.00	1.41	−0.81	ns
Typical appetite (1–10)	6.18	1.40	6.63	1.45	−0.95	ns
Eat more than intend to (1–10)	3.55	2.61	5.06	2.14	−1.90	ns
Flower picture ratings	1.00	0.16	1.01	0.04	−0.80	ns
Low-calorie picture ratings	3.63	1.35	3.83	1.36	−0.44	ns
High-calorie picture ratings	4.33	1.26	4.13	1.19	0.49	ns
Low-calorie picture memory	0.75	0.15	0.80	0.07	−1.19	ns
High-calorie picture memory	0.77	0.14	0.84	0.10	−1.76	ns

The table shows that there are no differences between men and women on demographic and performance variables. BMI = Body Mass Index; ESS = Epworth Sleepiness Scale; Current Hunger was rated on a 7-point scale (1 = not at all hungry; 7 = extremely hungry); Typical Appetite was rated on a 10-point scale (1 = never hungry; 10 = always hungry); Eat More than Intend to was rated on a 10-point scale (1 = never; 10 = always). Ratings refer to post-scan ratings taken for each image shown in the scanner. Participants responded to the question "how much you would like to eat each item right now" (1 = do not want to eat it; 7 = strongly desire to eat it). Memory scores indicate the proportion of correct recognition responses for each category of images (i.e., previously seen versus new foils) shown during the post-scan recognition test.

SD = 0.95 h). No sex differences were observed on any of these variables (see Table 1). All participants provided written informed consent prior to enrollment and were compensated for their time. This research study was approved by the McLean Hospital Institutional Review Board.

Materials and procedure

Each participant arrived for the study and underwent informed consent between 9:00 and 11:00 a.m. For the remainder of the morning, participants completed several self-report inventories, including questionnaires about demographic information, sleep habits, recent sleep, caffeine use, dietary intake, and appetite. In particular, participants were asked to respond to the query "what is your appetite like?" on a 10-point scale (*Appetite*: 1 = never hungry; 10 = always hungry), and to respond to the query "do you feel you eat more than you intend to" on a 10-point scale (*Overeating*: 1 = never; 10 = always). Participants also completed the Epworth Sleepiness Scale (ESS) (Johns, 1991), a self-report measure of general daytime sleepiness. The ESS is the most widely used self-report measure of general subjective sleepiness in the world (Drake, 2011) and shows high internal consistency reliability (Cronbach's alpha = 0.88) as well as high test-retest reliability ($r = 0.82$) over five months in healthy individuals (Johns, 1992). This scale requires the respondent to rate their chance of falling asleep in eight different situations (e.g. sitting and reading; as a passenger in a car for an hour without a break) in recent times along a 4-point scale (0 = would never doze, 1 = slight chance of dozing, 2 = moderate chance of dozing, 3 = high chance of dozing). Responses are summed to provide a total score (maximum: 24). Higher scores indicate greater general daytime sleepiness, and scores greater than 10 reflect excessive daytime sleepiness in the clinically significant range. Thus, the scale measures a general level of chronic propensity to fall asleep across a variety of settings rather than the acute level of sleepiness that may be measured with other state indices. This may allow greater unmasking of chronic sleep debt by focusing on the broader behavioral propensity for sleep than other measures of acute sleepiness (Pilcher et al., 2003). Participants were not restricted in their food consumption throughout the morning, but were required to document all intake for the day on a dietary log. No food was consumed within an hour prior to the functional neuroimaging scans.

Between 12:30 and 3:00 in the afternoon, participants underwent functional magnetic resonance imaging (fMRI) while completing a food perception task (FPT). The present task was a slightly modified version of the same task we have used in our prior work (Killgore and Yurgelun-Todd, 2005a,b, 2006, 2007, 2010; Killgore et al., 2003, 2010). During the FPT, participants viewed a series of 30-second blocks of images depicting high (H) calorie foods (e.g., cheeseburgers, French fries, cake, ice cream, candy), low calorie (L) foods (e.g., fresh salads, fruits, vegetables, fresh fish, whole grain bread), or control (C) images (i.e., non-edible rocks, flowers, shrubs). During each block, ten images were shown for three seconds each. The task included 15 s of resting fixation (+) at the beginning and end of the scan. The total duration of the FPT was 240 s and followed a constant presentation order (+, C, L, H, C, H, L, C, +) (see Supplementary Fig. 1). Participants were given the following instruction: "For this task, you will see a series of photographs. Try your best to remember the photographs, because your memory for the pictures will be tested after the scan." At the conclusion of the scan, participants completed a recognition task that presented all of the previously seen food items along with an equal number of distractor items. Following the recognition task, participants completed a 7-point rating scale to indicate their current level of hunger (i.e., 1 = not at all hungry; 7 = extremely hungry), and were then shown all of the previously seen food and control images. For each image, they were asked to rate "how much you would like to eat each item right now" (1 = do not want to eat it; 7 = strongly desire to eat it).

Magnetic resonance imaging parameters

Participants were scanned using a 3.0 Tesla SIEMENS Tim Trio scanner and a 12-channel head coil. At the outset, structural MRI scans were collected using a T1-weighted 3D MPRAGE sequence (TR/TE/flip angle = 2.1 s/2.25 ms/12°) over 128 sagittal slices (256 × 256 matrix) and a slice thickness of 1.33 mm, yielding a voxel size of 1 × 1 × 1.33 mm. During the FPT, a 4-minute blood oxygenation level dependent (BOLD) fMRI was acquired over 43 transverse interleaved slices using a T2*-weighted echo planar imaging sequence (TR/TE/flip angle = 3.0 s/30 ms/90°), with 80 images per slice (3.5 mm thickness, no skip; 22.4 cm field of view; 64 × 64 acquisition matrix), yielding a voxel size of 3.5 × 3.5 × 3.5 mm.

Image processing

The functional data were pre-processed and analyzed using standard algorithms in SPM5 (Wellcome Department of Cognitive Neurology, London, UK). For each subject, the time series of images was spatially realigned and motion corrected, co-registered to the individual's own anatomical image, spatially normalized to fit the template of the Montreal Neurological Institute (MNI), spatially smoothed using an isotropic Gaussian kernel (full width at half maximum [FWHM] = 6 mm), and resliced to 2 × 2 × 2 mm. Finally, the time series was also convolved with the canonical hemodynamic response function in SPM5, the effects of serial autocorrelation were removed using the first-level autoregressive model, and a high-pass filter of 128 s was used to remove low frequency drift in the signal.

Statistical analysis

The analysis proceeded in several stages. First, sex differences on questionnaire and behavioral indices were examined via independent samples t-tests. Next, zero-order correlations between behavioral variables, including total ESS, appetite, and overeating were examined for the sample as a whole and separately for women and men. Gender comparisons of correlations were undertaken with Fisher's r-to-z-transformation with comparison to a directional z-distribution. Third, the functional neuroimaging data were analyzed in a multi-stage process. At the initial stage, the primary effect of the calorie conditions within the food perception task was determined. This entailed constructing a general linear model for each individual that contrasted the difference in BOLD response between the high calorie and low calorie food conditions (see Supplementary Fig. 1). These contrast images were then taken to a second level random effects analysis via the multiple linear regression module of SPM5 to examine the relationship between total ESS scores and greater responsiveness of the brain to the high calorie condition of the FPT within the vmPFC. Based on our *a priori* hypotheses derived from previous research on the effects of sleep loss on brain function, we restricted the primary analyses to two bilateral search territories within a subregion of the ventromedial prefrontal cortex (i.e., left and right gyrus rectus) defined by the Automated Anatomical Labeling Atlas (Tzourio-Mazoyer et al., 2002) and implemented via the Wake Forest University PickAtlas Utility (Maldjian et al., 2003) as a toolbox in SPM5. Dilation factor for the utility was set to 0. Correlations were initially thresholded at $p < .001$, k (extent) ≥ 10 contiguous voxels, and then subjected to small volume correction for multiple comparisons within each search territory at $p < .05$, corrected for false discovery rate (FDR). Finally, to evaluate the relationship between sleepiness-related brain activation and eating behavior, mean signal intensity was extracted from each significant cluster of activation during the FPT and correlated with behavioral indices, including ratings for the items querying about typical appetite and eating more than intended. These relationships were examined separately for women and men. Differences in the magnitude of correlation coefficients between men

and women were evaluated via Fisher's r-to-z transformation against a directional z-distribution.

Results

Sex differences in questionnaire and eating behavioral indices

As evident in Table 1, women and men showed no significant differences in demographic, sleep, or appetite variables. Critically, there also was no sex difference in calories consumed on the day of the scan. During neuroimaging, both groups attended well to the task, with men ($M = 76\%$ correct, $SD = 14\%$; $t(21) = 8.61$, $p < .001$) and women ($M = 82\%$ correct, $SD = 8\%$; $t(21) = 16.74$, $p < .001$) scoring significantly above chance in their recognition of the previously seen food items after the scan.

Correlations between sleepiness and self-reported appetite/overeating behavior

Simple whole brain contrasts between food and control conditions and between High and Low Calorie conditions are presented in the online Supplementary Results (see Supplemental Fig. 2, and Supplemental Table 1 and 2). For the sample as a whole, ESS scores were positively correlated with typical appetite ratings ($r = .53$, $p = .001$), suggesting that greater general daytime sleepiness was associated with greater appetite. As evident in Fig. 1, this was true for men ($r = .44$, $p = .038$), but was nonsignificantly stronger for women ($r = .72$, $p = .002$)($z = -1.21$, $p = .11$). In contrast, ESS was not significantly correlated with the tendency to overeat ($r = .18$, $p = .29$), which did not differ for men ($r = .13$, $p = .58$) or women ($r = .37$, $p = .16$) ($z = -0.72$, $p = .24$). Similarly, ESS was not significantly correlated with current hunger at the time of the scan ($r = .24$, $p = .14$), and these nonsignificant relations were similar for men ($r = .23$, $p = .30$) and women ($r = .30$, $p = .26$) ($z = -0.21$, $p = .42$).

Correlations between sleepiness and brain responses

The correlation between ESS and brain responses to the High > Low Calorie contrast was evaluated for the entire sample as a whole. Within the search territories investigated, there were no regions that were significantly positively correlated with general daytime sleepiness scores. There was, however, a single cluster within the vmPFC that emerged as significantly negatively correlated with ESS scores. Fig. 2 shows the location of this cluster within the left gyrus rectus (MNI: $x = -8$, $y = 40$, $z = -20$; $k = 18$ voxels; $p = .047$ FDR small volume corrected). No other regions within the search territories were significantly correlated with ESS. To ensure that our findings were not driven by observations with extreme influence, we examined standardized residuals and leverage values. No standardized residuals exceeded 3.0, suggesting that none of the observations were extreme outliers. One observation exceeded threshold for leverage (i.e., $2(k+1)/n > 0.105$, where k = the number of predictors and n = sample size). With this observation removed, the correlation between the ESS and extracted parameter estimates for the left gyrus rectus cluster remained significant at $p < .01$. Furthermore, to determine whether this finding was influenced by current hunger or previous food ingestion, we correlated the mean signal intensity values of this region with these scores. Activation in this cluster was not correlated with hunger for the sample as a whole ($r = -.05$, $p = .79$), and this was true for both men ($r = -.10$, $p = .65$) and women ($r = .06$, $p = .84$) ($z = -0.45$, $p = .33$). Similarly, mean cluster activation was not significantly related to prior calorie consumption for the sample as a whole ($r = -.12$, $p = .46$), a finding that was similar among men ($r = -.13$, $p = .55$) and women ($r = -.04$, $p = .90$) ($z = -0.25$, $p = .40$).

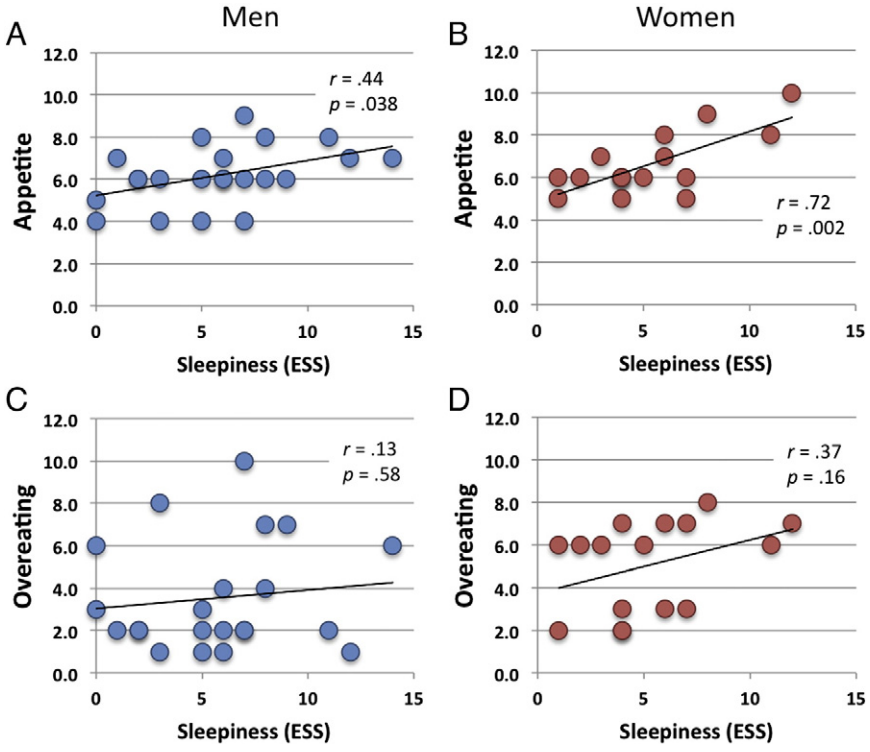


Fig. 1. Scatterplots showing the association between general daytime sleepiness on the Epworth Sleepiness Scale (ESS) and eating-related variables separately for men and women. Daytime sleepiness was significantly correlated with general appetite ratings for both A) men and B) women. In contrast, there was no significant correlation between general daytime sleepiness scores and the tendency to overeat among C) men or D) women.

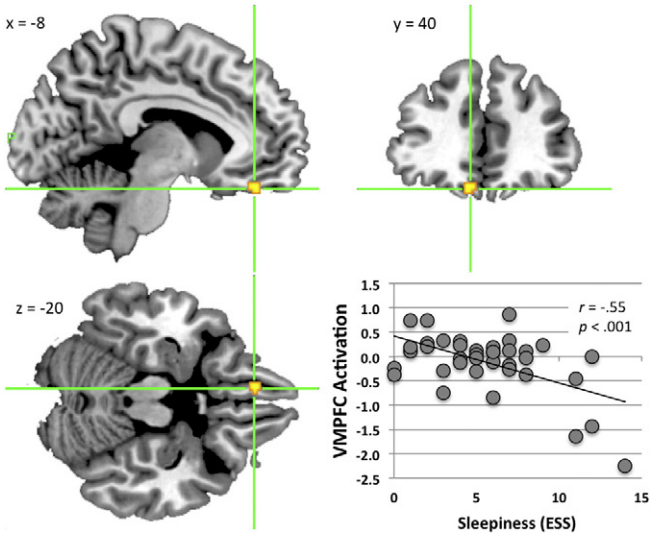


Fig. 2. Daytime sleepiness ratings on the Epworth Sleepiness Scale (ESS) were significantly negatively correlated ($p<.05$, FDR) with a cluster of activation within the ventromedial prefrontal cortex (vmPFC), at the location of the left gyrus rectus (cluster size = 18 voxels). The cluster of activation is shown in the sagittal (top left), coronal (top right), and axial (bottom left) views. The scatter plot (bottom right) shows the association between ESS scores and the mean beta values extracted from the activated cluster [MNI: −8, 40, −20].

Correlations between brain responses and self-reported appetite/overeating behavior

The mean beta values from the cluster identified above were extracted for each individual and correlated with self-reported appetite and overeating behavior. For the sample as a whole, there was no significant relationship between vmPFC activation and appetite ($r=-.22$, $p=.18$) for either men ($r=-.29$, $p=.19$) or women ($r=-.28$, $p=.29$) ($z=-0.03$, $p=.49$). With regard to overeating, there was also no significant relationship with the vmPFC for the sample as a whole ($r=.24$, $p=.14$). However, men and women appeared to differ in this response pattern (see Fig. 3). While men showed no significant association between vmPFC activation and self-reported overeating ($r=.10$, $p=.65$), women showed a significant negative correlation ($r=-.52$, $p=.04$), a difference that was statistically significant ($z=1.88$, $p=.03$), suggesting that reduced responsiveness of this region during food perception was associated with a greater tendency to eat more than intended.

Discussion

We found that self-reported daytime sleepiness was associated with several factors that could lead to excessive food consumption. First, general daytime sleepiness, as assessed by the ESS, was associated with increased ratings of global appetite. Second, when participants were confronted with images of enticing high-calorie foods during neuroimaging, general daytime sleepiness was also associated with reduced activation within a cluster located within the vmPFC, a brain region involved in the ability to inhibit and control emotions and behavior. Third, this reduction in prefrontal activation was directly predictive of self-reported difficulty curtailing food intake, although this association was only significant for women. These findings add to a growing literature suggesting that insufficient sleep and its sequelae are associated with weight gain and the development of obesity (Patel, 2009; Van Cauter and Knutson, 2008), but also sheds light on some additional neurobiological mechanisms in this process that may have heretofore been overlooked.

Recent reviews of the literature have proposed several key physiological mechanisms through which short sleep duration is likely to

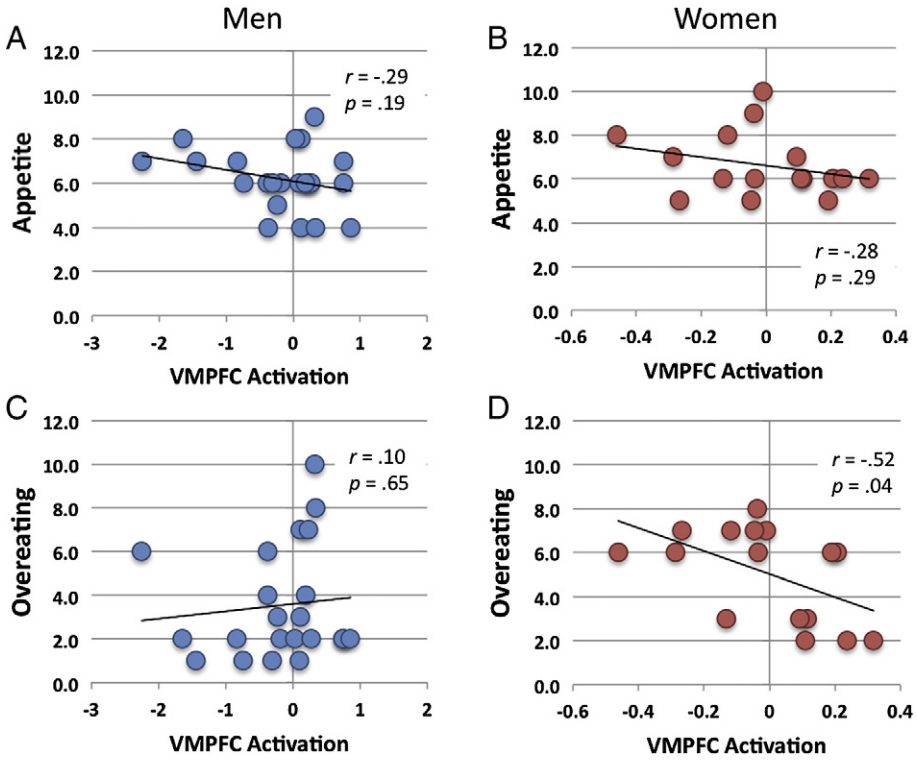


Fig. 3. Scatterplots showing the association between the mean extracted beta values from the ventromedial prefrontal cortex (vmPFC) cluster [MNI: −8, 40, −20] and eating related variables separately for men and women. Activation in the vmPFC was not significantly correlated with general appetite ratings for either A) men or B) women. However, while there was no significant correlation between vmPFC activation and the tendency to overeat among C) men, activation within this cluster was significantly negatively correlated with overeating among D) women.

contribute to increased risk for obesity and diabetes (Knutson et al., 2007; Van Cauter et al., 2008). Most current hypothesized models propose that sleep curtailment leads to 1) increased calorie intake due to alterations in the balance of appetite related hormones and more time available to eat, and 2) reduced energy expenditure due to increased fatigue and altered thermoregulation (Knutson et al., 2007; Patel and Hu, 2008). A prominent feature of these models is evidence that sleep loss exerts a powerful influence on the balance of the hormones that regulate hunger and food consumption, including the appetite stimulating hormone ghrelin and the appetite suppressing hormone leptin (Gale et al., 2004; van der Lely et al., 2004). One large scale study with over a thousand participants showed that polysomnographically measured sleep during an overnight laboratory stay was positively correlated with leptin and negatively correlated with ghrelin levels measured from blood samples the next morning (Taheri et al., 2004). In rodents, laboratory sleep deprivation leads to excessive food consumption (Rechtschaffen and Bergmann, 1995), and studies in humans also suggest that sleep deprivation leads to increased appetite, hunger (Benedict et al., 2012; Pejovic et al., 2010; Spiegel et al., 2004), total food intake (Brondel et al., 2010), and snacking on empty calories (Nedeltcheva et al., 2009). Such findings have led many researchers to suggest that these physiological changes following short sleep duration may contribute to the propensity toward overweight and obesity (Knutson et al., 2007; Patel, 2009; Patel and Hu, 2008; Patel et al., 2008; Van Cauter and Knutson, 2008; Van Cauter et al., 2008).

While physiological factors such as altered leptin and ghrelin levels and reduced energy expenditure appear to play key roles in food intake following sleep loss, the present findings suggest an additional effect of chronically insufficient sleep that may also contribute to overeating. Specifically, we found that higher levels of general daytime sleepiness, as measured by the ESS, were associated with reduced responsiveness of a small cluster within vmPFC when exposed to visual images depicting unhealthy high-calorie foods. This region of the brain has been shown to be critical to a number of emotional and behavioral functions that may directly affect appetitive behavior, including inhibitory capacity (Hodgson et al., 2002; Hornberger et al., 2011; Silbersweig et al., 2007; Szatkowska et al., 2007), representation of the affective value of stimuli (Doallo et al., 2012), and the ability to suppress short-term gains in the service of obtaining longer-term advantageous outcomes (Bechara, 2004; Bechara et al., 2000). Damage to this region has been associated with shortsighted decision-making (Bechara et al., 1994) and problems inhibiting behavior (Hornberger et al., 2011; Szatkowska et al., 2007). Moreover, we found that the lower the activation within this region of the brain, the greater the self-reported tendency to overeat. Thus, not only does lack of sleep affect the metabolic energy balance and hormonal regulators that contribute to increased hunger or appetite, but general daytime sleepiness itself appears to be associated with reduced functional activation within an inhibitory brain region that is critical for regulating behavior, a decline which in turn relates to excessive food consumption.

These findings are consistent with evidence from studies of the effects of laboratory-based sleep deprivation on brain functioning and behavioral control. Studies using PET imaging have demonstrated reduced regional glucose metabolism within the vmPFC following as little as one night of sleep loss (Thomas et al., 2000; Wu et al., 2006). This alteration in brain function within inhibitory and emotional control regions following sleep deprivation corresponds with increased impulsiveness and risk-taking behavior. For example, behavioral studies have shown that sleep deprivation is associated with reduced inhibitory capacity on a go/no-go task (Drummond et al., 2006), short-sighted preference for immediate risky gains over the potential for greater long-term losses (Killgore et al., 2006, 2012a), increased impulsive risk-taking (Killgore, 2007; Killgore et al., 2011), and a bias for risky choices when the outcome is viewed in terms of potential gains rather than losses (McKenna et al., 2007). Overall, sleep deprived individuals tend to show a greater expectation that their risky decisions will lead to gains and a diminished expectation for losses (Venkatraman et al., 2007). Additionally, during sleep deprivation, individuals begin to shift their decision-making strategies away from a focus on avoiding losses toward one of seeking increased gains, a pattern that also involves changes in the activation of the vmPFC (Venkatraman et al., 2011). Evidence also suggests that sleep loss alters the economic value ascribed to stimuli, increasing the perceived reward value of stimuli for some individuals while decreasing it for others (Libedinsky et al., 2011), a pattern that correlates significantly with changes in the activation of the vmPFC following sleep deprivation. When interpreted in light of these prior studies, the inverse relationship between general sleepiness and prefrontal activation we observed suggests that generally sleepy individuals may experience reduced ability to inhibit impulses to eat high calorie foods or they may show increased valuation or expectation of reward from such foods relative to their less sleepy counterparts. Future research will be necessary to determine the relative contribution of prefrontal disinhibition versus altered reward value in the tendency to overeat among individuals with chronically elevated levels of sleepiness.

Interestingly, whereas greater general daytime sleepiness was associated with increased appetite ratings for both sexes, we found that the correlation between food-specific brain responses and self-reported overeating was present only among women, despite similar levels of overeating between sexes overall. These findings are consistent with recent evidence suggesting that women and men may differ in their ability to inhibit activation of the orbitofrontal cortex and suppress corresponding feelings of hunger (Wang et al., 2009). Such findings have previously been proposed as one contributing factor to the higher rates of obesity and eating disorders among women (Hoek, 2006; Striegel-Moore and Bulik, 2007; Striegel-Moore et al., 2009). Prior studies have suggested that women tend to report greater loss of control when eating (Striegel-Moore et al., 2009), a finding that comports well with our results showing that sleepiness-related reductions in prefrontal activation in women were associated with the tendency to eat more than intended. Recent research has also shown that men and women respond differently to high- and low-calorie food stimuli, with women tending to show stronger activation in the insular cortex than men in response to high calorie foods (Killgore and Yurgelun-Todd, 2010). Other studies have also suggested that women show greater activation of dorsolateral prefrontal regions to hedonic foods (Cornier et al., 2010), and greater responsiveness of visual processing regions than men when in a hungry versus sated state (Frank et al., 2010). The precise cause of these sex differences in brain responsiveness still remain elusive, but it seems likely that such distinctions may relate to differences in gonadal sex hormones, which appear to have significant effects on a number of neurological and physiological systems related to food consumption, particularly with regard to the regulation of insulin and leptin (Woods et al., 2003). Further research aimed at addressing the underlying sex differences in responses to food stimuli and the role which sleep may play in this process will be critical in addressing the urgent problem of rising rates of obesity in Western cultures.

While the present study suggests that general daytime sleepiness is related to the functioning of prefrontal regions important to behavioral control and eating behavior, several limitations of this research should be considered. First, we explored the construct of general subjective "sleepiness" rather than short sleep duration or total sleep deprivation. While sleepiness is a common outcome of insufficient sleep, the two constructs are not directly interchangeable. Second, general sleepiness on the ESS reflects a stable assessment of the propensity for sleep to occur across a variety of settings relative to "acute sleepiness" as assessed by other state measures of immediate sleepiness, which were not used here. Of course, there may be measurement error and recall biases inherent in any such subjective measure which queries about recent experience. The present findings can only be

validly generalized to general or chronic levels of sleepiness that tend to emerge with accumulated sleep debt over time, as is generally assessed with the ESS. Third, participants in this study were not selected for weight status, and we specifically screened out individuals with a history of psychopathology, including eating disorders. Consequently, these findings may not generalize to individuals with eating disorders or problems with obesity. Further research with such populations would be an important extension of this work. Fourth, based on prior research suggesting that the vmPFC may be a particularly important region affected by short sleep duration, we focused specifically on that region. Obviously, other regions or networks, such as reward circuitry, interoceptive signaling systems, emotional processing, and visual perception regions, may also be important and should be explored in future research. Fifth, our study lacked any assays for appetite-related hormones such as leptin and ghrelin, so it is not possible to directly rule out the influence of these factors on performance. Lastly, rather than having our participants tested following a fasting period, we opted to have them assessed following their normal daily intake of food during the morning. Nonetheless, energy consumption was monitored closely via food logs, and no food was consumed within an hour before the scanning. Although we controlled for the effects of caloric intake in our analyses, it is possible that the findings may have been different if participants were tested in a strictly fasting or sated state. With due consideration of these potential limitations, we believe the present study provides important new data regarding the role of general daytime sleepiness on brain responses to high-calorie, unhealthy foods. These findings suggest that, in addition to the effects of sleep loss on hormonal levels and energy balance, general daytime sleepiness may also affect brain regions that are critical to the ability to make effective decisions, regulate emotions, and inhibit behavior. Such altered brain functioning due to sleepiness may be an additional and potentially modifiable factor that contributes to the current epidemic of obesity.

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.neuroimage.2013.01.018.

Conflicts of interest

None declared.

References

Bechara, A., 2004. The role of emotion in decision-making: evidence from neurological patients with orbitofrontal damage. Brain Cogn. 55, 30–40.

Bechara, A., Damasio, A.R., Damasio, H., Anderson, S.W., 1994. Insensitivity to future consequences following damage to human prefrontal cortex. Cognition 50, 7–15.

Bechara, A., Damasio, H., Damasio, A.R., 2000. Emotion, decision making and the orbitofrontal cortex. Cereb. Cortex 10, 295–307.

Benedict, C., Brooks, S.J., O'Daly, O.G., Almen, M.S., Morell, A., Aberg, K., Gingnell, M., Schultes, B., Hallschmid, M., Broman, J.E., Larsson, E.M., Schioth, H.B., 2012. Acute sleep deprivation enhances the brain's response to hedonic food stimuli: an fMRI study. J. Clin. Endocrinol. Metab. 97, E443–E447.

Blasi, G., Goldberg, T.E., Weickert, T., Das, S., Kohn, P., Zoltick, B., Bertolino, A., Callicott, J.H., Weinberger, D.R., Mattay, V.S., 2006. Brain regions underlying response inhibition and interference monitoring and suppression. Eur. J. Neurosci. 23, 1658–1664.

Brondel, L., Romer, M.A., Nougues, P.M., Touyarou, P., Davenne, D., 2010. Acute partial sleep deprivation increases food intake in healthy men. Am. J. Clin. Nutr. 91, 1550–1559.

Center for Disease Control and Prevention, 2012. Short sleep duration among workers—United States, 2010. Morbidity and Mortality Weekly Report. U.S. Government Printing Office, Washington, pp. 281–285.

Cornier, M.A., Salzberg, A.K., Endly, D.C., Bessesen, D.H., Tregellas, J.R., 2010. Sex-based differences in the behavioral and neuronal responses to food. Physiol. Behav. 99, 538–543.

De Havas, J.A., Parimal, S., Soon, C.S., Chee, M.W., 2012. Sleep deprivation reduces default mode network connectivity and anti-correlation during rest and task performance. NeuroImage 59, 1745–1751.

Doallo, S., Raymond, J.E., Shapiro, K.L., Kiss, M., Eimer, M., Nobre, A.C., 2012. Response inhibition results in the emotional devaluation of faces: neural correlates as revealed by fMRI. Soc. Cogn. Affect. Neurosci. 7, 649–659.

Drake, C.L., 2011. Subjective measures of sleepiness. In: Thorpy, M.J., Billiard, M. (Eds.), Sleepiness: Causes, Consequence and Treatment. Cambridge University Press, New York, pp. 60–71.

Drummond, S.P., Paulus, M.P., Tapert, S.F., 2006. Effects of two nights sleep deprivation and two nights recovery sleep on response inhibition. J. Sleep Res. 15, 261–265.

Flegal, K.M., Carroll, M.D., Ogden, C.L., Johnson, C.L., 2002. Prevalence and trends in obesity among US adults, 1999–2000. JAMA 288, 1723–1727.

Frank, S., Laharnar, N., Kullmann, S., Veit, R., Canova, C., Hegner, Y.L., Fritsche, A., Preissl, H., 2010. Processing of food pictures: influence of hunger, gender and calorie content. Brain Res. 1350, 159–166.

Gale, S.M., Castracane, V.D., Mantzoros, C.S., 2004. Energy homeostasis, obesity and eating disorders: recent advances in endocrinology. J. Nutr. 134, 295–298.

Gallup Organization, 1995. Sleep in America.

Gangwisch, J.E., Malaspina, D., Boden-Albala, B., Heymsfield, S.B., 2005. Inadequate sleep as a risk factor for obesity: analyses of the NHANES I. Sleep 28, 1289–1296.

Hariri, A.R., Mattay, V.S., Tessitore, A., Fera, F., Weinberger, D.R., 2003. Neocortical modulation of the amygdala response to fearful stimuli. Biol. Psychiatry 53, 494–501.

Harrison, Y., Horne, J.A., 2000. The impact of sleep deprivation on decision making: a review. J. Exp. Psychol. Appl. 6, 236–249.

Hasler, G., Buysse, D.J., Klaghofer, R., Gamma, A., Ajdacic, V., Eich, D., Rossler, W., Angst, J., 2004. The association between short sleep duration and obesity in young adults: a 13-year prospective study. Sleep 27, 661–666.

Hodgson, T.L., Mort, D., Chamberlain, M.M., Hutton, S.B., O'Neill, K.S., Kennard, C., 2002. Orbitofrontal cortex mediates inhibition of return. Neuropsychologia 40, 1891–1901.

Hoek, H.W., 2006. Incidence, prevalence and mortality of anorexia nervosa and other eating disorders. Curr. Opin. Psychiatry 19, 389–394.

Hornberger, M., Geng, J., Hodges, J.R., 2011. Convergent grey and white matter evidence of orbitofrontal cortex changes related to disinhibition in behavioural variant frontotemporal dementia. Brain 134, 2502–2512.

Johns, M.W., 1991. A new method for measuring daytime sleepiness: the Epworth Sleepiness Scale. Sleep 14, 540–545.

Johns, M.W., 1992. Reliability and factor analysis of the Epworth Sleepiness Scale. Sleep 15, 376–381.

Killgore, W.D.S., 2007. Effects of sleep deprivation and morningness–eveningness traits on risk-taking. Psychol. Rep. 100, 613–626.

Killgore, W.D.S., 2010. Effects of sleep deprivation on cognition. Prog. Brain Res. 185, 105–129.

Killgore, W.D.S., Yurgelun-Todd, D.A., 2005a. Body mass predicts orbitofrontal activity during visual presentations of high-calorie foods. Neuroreport 16, 859–863.

Killgore, W.D.S., Yurgelun-Todd, D.A., 2005b. Developmental changes in the functional brain responses of adolescents to images of high and low-calorie foods. Dev. Psychobiol. 47, 377–397.

Killgore, W.D.S., Yurgelun-Todd, D.A., 2006. Affect modulates appetite-related brain activity to images of food. Int. J. Eat. Disord. 39, 357–363.

Killgore, W.D.S., Yurgelun-Todd, D.A., 2007. Positive affect modulates activity in the visual cortex to images of high calorie foods. Int. J. Neurosci. 117, 643–653.

Killgore, W.D.S., Yurgelun-Todd, D.A., 2010. Sex differences in cerebral responses to images of high versus low-calorie food. Neuroreport 21, 354–358.

Killgore, W.D.S., Young, A.D., Femia, L.A., Bogorodzki, P., Rogowska, J., Yurgelun-Todd, D.A., 2003. Cortical and limbic activation during viewing of high- versus low-calorie foods. NeuroImage 19, 1381–1394.

Killgore, W.D.S., Balkin, T.J., Wesensten, N.J., 2006. Impaired decision-making following 49 hours of sleep deprivation. J. Sleep Res. 15, 7–13.

Killgore, W.D.S., Ross, A.J., Kamiya, T., Kawada, Y., Renshaw, P.F., Yurgelun-Todd, D.A., 2010. Citicoline affects appetite and cortico-limbic responses to images of high-calorie foods. Int. J. Eat. Disord. 43, 6–13.

Killgore, W.D., Kamimori, G.H., Balkin, T.J., 2011. Caffeine protects against increased risk-taking propensity during severe sleep deprivation. J. Sleep Res. 20, 395–403.

Killgore, W.D., Grugle, N.L., Balkin, T.J., 2012a. Gambling when sleep deprived: don't bet on stimulants. Chronobiol. Int. 29, 43–54.

Killgore, W.D., Schwab, Z.J., Kipman, M., Deldonno, S.R., Weber, M., 2012b. Voxel-based morphometric gray matter correlates of daytime sleepiness. Neurosci. Lett. 518, 10–13.

Killgore, W.D., Schwab, Z.J., Weiner, M.R., 2012c. Self-reported nocturnal sleep duration is associated with next-day resting state functional connectivity. Neuroreport 23, 741–745.

Knutson, K.L., Spiegel, K., Penev, P., Van Cauter, E., 2007. The metabolic consequences of sleep deprivation. Sleep Med. Rev. 11, 163–178.

Kripke, D.F., Simons, R.N., Garfinkel, L., Hammond, E.C., 1979. Short and long sleep and sleeping pills. Is increased mortality associated? Arch. Gen. Psychiatry 36, 103–116.

Lewinsohn, P.M., Seeley, J.R., Moerk, K.C., Striegel-Moore, R.H., 2002. Gender differences in eating disorder symptoms in young adults. Int. J. Eat. Disord. 32, 426–440.

Libedinsky, C., Smith, D.V., Teng, C.S., Namburi, P., Chen, V.W., Huettel, S.A., Chee, M.W., 2011. Sleep deprivation alters valuation signals in the ventromedial prefrontal cortex. Front. Behav. Neurosci. 5, 70.

Maldjian, J.A., Laurienti, P.J., Kraft, R.A., Burdette, J.H., 2003. An automated method for neuroanatomic and cytoarchitectonic atlas-based interrogation of fMRI data sets. NeuroImage 19, 1233–1239.

McKenna, B.S., Dickinson, D.L., Orff, H.J., Drummond, S.P., 2007. The effects of one night of sleep deprivation on known-risk and ambiguous-risk decisions. J. Sleep Res. 16, 245–252.

Middelkoop, H.A., Smilde-van den Doel, D.A., Neven, A.K., Kamphuisen, H.A., Springer, C.P., 1996. Subjective sleep characteristics of 1,485 males and females aged 50–93: effects of sex and age, and factors related to self-evaluated quality of sleep. J. Gerontol. A Biol. Sci. Med. Sci. 51, M108–M115.

National Sleep Foundation, 2005. Sleep in America Poll. National Sleep Foundation, Washington.

National Sleep Foundation, 2007. Sleep in America Poll. National Sleep Foundation, Washington.

Nedeltcheva, A.V., Kilkus, J.M., Imperial, J., Kasza, K., Schoeller, D.A., Penev, P.D., 2009. Sleep curtailment is accompanied by increased intake of calories from snacks. Am. J. Clin. Nutr. 89, 126–133.

O'Connor, C., Thornley, K.S., Hanly, P.J., 2000. Gender differences in the polysomnographic features of obstructive sleep apnea. Am. J. Respir. Cri.t Care Med. 161, 1465–1472.
Ogden, C.L., Carroll, M.D., Curtin, L.R., McDowell, M.A., Tabak, C.J., Flegal, K.M., 2006. Prevalence of overweight and obesity in the United States, 1999–2004. JAMA 295, 1549–1555.
Ogden, C.L., Carroll, M.D., Kit, B.K., Flegal, K.M., 2012. Prevalence of obesity in the United States, 2009–2010. NCHS data brief, pp. 1–8.
Patel, S.R., 2009. Reduced sleep as an obesity risk factor. Obes. Rev. 10 (Suppl. 2), 61–68.
Patel, S.R., Hu, F.B., 2008. Short sleep duration and weight gain: a systematic review. Obesity 16, 643–653.
Patel, S.R., Blackwell, T., Redline, S., Ancoli-Israel, S., Cauley, J.A., Hillier, T.A., Lewis, C.E., Orwoll, E.S., Stefanick, M.L., Taylor, B.C., Yaffe, K., Stone, K.L., 2008. The association between sleep duration and obesity in older adults. Int. J. Obes. 32, 1825–1834.
Paulus, M.P., Frank, L.R., 2003. Ventromedial prefrontal cortex activation is critical for preference judgments. Neuroreport 14, 1311–1315.
Pejovic, S., Vgontzas, A.N., Basta, M., Tsaoussoglou, M., Zoumakis, E., Vgontzas, A., Bixler, E.O., Chrousos, G.P., 2010. Leptin and hunger levels in young healthy adults after one night of sleep loss. J. Sleep Res. 19, 552–558.
Pilcher, J.J., Pury, C.L., Muth, E.R., 2003. Assessing subjective daytime sleepiness: an internal state versus behavior approach. Behav. Med. 29, 60–67.
Rechtschaffen, A., Bergmann, B.M., 1995. Sleep deprivation in the rat by the disk-over-water method. Behav. Brain Res. 69, 55–63.
Ridderinkhof, K.R., van den Wildenberg, W.P., Segalowitz, S.J., Carter, C.S., 2004. Neurocognitive mechanisms of cognitive control: the role of prefrontal cortex in action selection, response inhibition, performance monitoring, and reward-based learning. Brain Cogn. 56, 129–140.
Samann, P.G., Tully, C., Spoormaker, V.I., Wetter, T.C., Holsboer, F., Wehrle, R., Czisch, M., 2010. Increased sleep pressure reduces resting state functional connectivity. MAGMA 23, 375–389.
Silbersweig, D., Clarkin, J.F., Goldstein, M., Kernberg, O.F., Tuescher, O., Levy, K.N., Brendel, G., Pan, H., Beutel, M., Pavony, M.T., Epstein, J., Lenzenweger, M.F., Thomas, K.M., Posner, M.I., Stern, E., 2007. Failure of frontolimbic inhibitory function in the context of negative emotion in borderline personality disorder. Am. J. Psychiatry 164, 1832–1841.
Spiegel, K., Tasali, E., Penev, P., Van Cauter, E., 2004. Brief communication: Sleep curtailment in healthy young men is associated with decreased leptin levels, elevated ghrelin levels, and increased hunger and appetite. Ann. Intern. Med. 141, 846–850.
Striegel-Moore, R.H., Bulik, C.M., 2007. Risk factors for eating disorders. Am. Psychol. 62, 181–198.
Striegel-Moore, R.H., Rosselli, F., Perrin, N., DeBar, L., Wilson, G.T., May, A., Kraemer, H.C., 2009. Gender difference in the prevalence of eating disorder symptoms. Int. J. Eat. Disord. 42, 471–474.
Szatkowska, I., Szymanska, O., Bojarski, P., Grabowska, A., 2007. Cognitive inhibition in patients with medial orbitofrontal damage. Exp. Brain Res. (Experimentelle Hirnforschung. Experimentation cerebrale) 181, 109–115.
Taheri, S., Lin, L., Austin, D., Young, T., Mignot, E., 2004. Short sleep duration is associated with reduced leptin, elevated ghrelin, and increased body mass index. PLoS Med. 1, e62.
Thomas, M., Sing, H., Belenky, G., Holcomb, H., Mayberg, H., Dannals, R., Wagner, H., Thorne, D., Popp, K., Rowland, L., Welsh, A., Balwinski, S., Redmond, D., 2000. Neural basis of alertness and cognitive performance impairments during sleepiness. I. Effects of 24 h of sleep deprivation on waking human regional brain activity. J. Sleep Res. 9, 335–352.
Tzourio-Mazoyer, N., Landeau, B., Papathanassiou, D., Crivello, F., Etard, O., Delcroix, N., Mazoyer, B., Joliot, M., 2002. Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. NeuroImage 15, 273–289.
Van Cauter, E., Knutson, K.L., 2008. Sleep and the epidemic of obesity in children and adults. Eur. J. Endocrinol. 159 (Suppl. 1), S59–S66.
Van Cauter, E., Spiegel, K., Tasali, E., Leproult, R., 2008. Metabolic consequences of sleep and sleep loss. Sleep Med. 9 (Suppl. 1), S23–S28.
van der Lely, A.J., Tschop, M., Heiman, M.L., Ghigo, E., 2004. Biological, physiological, pathophysiological, and pharmacological aspects of ghrelin. Endocr. Rev. 25, 426–457.
Venkatraman, V., Chuah, Y.M., Huettel, S.A., Chee, M.W., 2007. Sleep deprivation elevates expectation of gains and attenuates response to losses following risky decisions. Sleep 30, 603–609.
Venkatraman, V., Huettel, S.A., Chuah, L.Y., Payne, J.W., Chee, M.W., 2011. Sleep deprivation biases the neural mechanisms underlying economic preferences. J. Neurosci. 31, 3712–3718.
Wang, G.J., Volkow, N.D., Telang, F., Jayne, M., Ma, Y., Pradhan, K., Zhu, W., Wong, C.T., Thanos, P.K., Geliebter, A., Biegon, A., Fowler, J.S., 2009. Evidence of gender differences in the ability to inhibit brain activation elicited by food stimulation. Proc. Natl. Acad. Sci. U. S. A. 106, 1249–1254.
Woods, S.C., Gotoh, K., Clegg, D.J., 2003. Gender differences in the control of energy homeostasis. Exp. Biol. Med. 228, 1175–1180.
Wu, J.C., Gillin, J.C., Buchsbaum, M.S., Chen, P., Keator, D.B., Khosla Wu, N., Darnall, L.A., Fallon, J.H., Bunney, W.E., 2006. Frontal lobe metabolic decreases with sleep deprivation not totally reversed by recovery sleep. Neuropsychopharmacology 31, 2783–2792.
Yoo, S.S., Gujar, N., Hu, P., Jolesz, F.A., Walker, M.P., 2007. The human emotional brain without sleep—a prefrontal amygdala disconnect. Curr. Biol. 17, R877–R878.
Zhang, B., Wing, Y.K., 2006. Sex differences in insomnia: a meta-analysis. Sleep 29, 85–93.

International Journal of Obesity (2013), 1–8

www.nature.com/ijo

ORIGINAL ARTICLE

Cortico-limbic responsiveness to high-calorie food images predicts weight status among women

WDS Killgore, M Weber, ZJ Schwab, M Kipman, SR DelDonno, CA Webb and SL Rauch

OBJECTIVES: Excessive weight gain and obesity are currently among the world's major threats to health. Women show significantly higher rates of obesity and eating disorders relative to men, but the factors contributing to these gender differences remain uncertain. We examined the correlations between regional brain responses to images of high-calorie versus low-calorie foods and self-reported motivational status, including ratings of general appetite, overeating propensity, state hunger and desire for specific foods.
SUBJECTS: Thirty-eight healthy right-handed adults (22 male; 16 female) ages 18–45 participated. There were no differences between males and females with regard to age or body mass index (BMI).
RESULTS: Overall, motivational status correlated significantly with activation within the amygdala, insula and orbitofrontal cortex. Regional activation was then used to predict BMI, an indicator of long-term food consumption and energy expenditure. The combined model was significant, accounting for 76% of the variance in BMI for women, whereas the same regions were not predictive of weight status among men.
CONCLUSIONS: Findings suggest that long-term weight status is related to visual responsiveness to calorie-dense food imagery among women.

International Journal of Obesity advance online publication, 5 March 2013; doi:10.1038/ijo.2013.26

Keywords: food; appetite; sex differences; fMRI; neuroimaging

INTRODUCTION

Problems with overweight and obesity are currently among the major public health concerns facing westernized societies. Within the United States, 2 of every 3 adults are classified as overweight,[1] and over 1 in 3 now meet criteria for obesity.[2] Excess weight gain is associated with numerous long-term health problems, including increased risk of type 2 diabetes, hypertension, stroke, cardiovascular disease, and a range of other negative health outcomes.[3] In addition, those meeting criteria for obesity are twice as likely than their normal weight peers to succumb to premature death from a variety of causes.[3] Women, in particular, appear to show the greatest problems with excess weight gain,[2] extreme obesity,[4] and higher rates of eating disorders relative to men.[5–7] Food consumption and weight gain among humans is an extraordinarily complex phenomenon, regulated by genetic,[8] central,[9] and peripheral neurobiological factors,[10] as well as complex social, cognitive and psychological variables.[11–14] Consequently, the basis for these sex differences in weight gain and food consumption remain unclear, but some evidence suggests that there are distinctions between men and women in their behavioral responses to food stimuli,[7] and even in the responsiveness of critical brain regions involved in regulating appetite and food intake.[15,16]

Individuals vary in their motivational status and behavioral control when confronted with food stimuli.[17] Incentive to consume food in the immediate environment is dictated by an individual's current hunger state[18] and general hedonic preference for specific foods.[19,20] While the long-term ability to regulate food consumption and to maintain a stable weight is associated with individual hedonic preferences for food stimuli, it may also be related to a general capacity to inhibit behavior and affective responses.[21] In particular, the ability to modulate behavior in response to tempting food is strongly linked to several aspects of impulse control, such as executive attention, inhibitory control and affect regulation,[22] capacities that are often associated with the behavioral[23] and emotion[24] regulation functions of the prefrontal cortex. The medial orbitofrontal cortex, in particular, appears to be one among several nodes within a complex neurocircuitry involved in responding to food stimuli[25–29] and regulating food intake,[30,31] a system that also likely includes the amygdala and posterior insula, among others. In the present study, we used functional magnetic resonance imaging (fMRI) to examine the responsiveness of this system to visual images of unhealthy high-calorie versus relatively healthy low-calorie foods, and correlated that activation with several self-report variables important to food motivation, including general appetite level (*Appetite*), the propensity to overeat (*Overeating*), state hunger (*Hunger*), and hedonic attraction to the individual foods (*Food Desire*). Based on prior research described above, we restricted our primary analyses to the amygdala, insula and medial orbitofrontal cortex. Activation within the regions found to be related to each of these food motivational indices was then used to predict body mass index (BMI), a stable measure of long-term food consumption. Based on our prior findings that cerebral responses to images of food stimuli were stronger in women than men,[16] and similar findings reported by others,[15] we hypothesized that such responses would be related to BMI among women, but would be weaker or non-existent among men.

Social, Cognitive and Affective Neuroscience Lab, McLean Hospital, Harvard Medical School, Belmont, MA, USA. Correspondence: Dr WDS Killgore, Social, Cognitive, and Affective Neuroscience Lab, McLean Hospital, Harvard Medical School, 115 Mill Street, Belmont, MA 02478, USA.
E-mail: killgore@mclean.harvard.edu
Received 19 November 2012; revised 21 January 2013; accepted 28 January 2013

MATERIALS AND METHODS

Participants

The participants included thirty-eight healthy right-handed adults (22 male; 16 female) recruited via internet advertisements and posted flyers from the Boston metropolitan region, ranging in age from 18 to 45 years ($M = 30.1$, $s.d. = 8.3$). There were no differences between males ($M = 31.5$, $s.d. = 9.3$) and females ($M = 28.3$, $s.d. = 7.5$) with regard to age. A trained research technician screened all potential volunteers during a semi-structured telephone interview. Based on this screening, enrolled participants were deemed to be free from any history of severe medical conditions, head injury, loss of consciousness >30 min, brain tumors, seizures, neurologic conditions, symptoms consistent with Axis I psychopathology, or drug or alcohol treatment. Additionally, potential participants were excluded for current or recent use of any psychoactive medications, illicit substances or excessive alcohol intake. Normal or corrected normal visual acuity with contact lenses was required. BMI was determined through self-reported height and weight recorded on the prescan questionnaire. Men and women ranged from low normal BMI to Stage I obesity (males = 24.24, $s.d. = 3.60$, range = 19.80–33.47; females = 25.08, $s.d. = 4.01$; range = 19.84–34.78), which did not differ significantly between the groups. Written informed consent was obtained before enrollment and all participants were compensated for their time. This research study was reviewed and approved by the McLean Hospital Institutional Review Board.

Materials and procedure

Informed consent and prescan procedures began for each participant between 0900 and 1100 hours, during which participants completed a number of self-report inventories querying about demographic information, dietary intake and appetite/food consumption behavior. For the present analysis, participants answered the following questions: (1) 'what is your appetite like?' on a 10-point scale (*Appetite*: 1 = never hungry; 10 = always hungry), and (2) 'do you feel you eat more than you intend to' on a 10-point scale (*Overeating*: 1 = never; 10 = always). In order to ensure some variability in hunger ratings, participants were permitted to consume food if desired throughout the prescan period, although all intake throughout the day was documented on a food diary. However, no food was permitted for an hour before the fMRI scans. Men and women did not differ on any of these scales (all *P*-values >0.05).

Functional neuroimaging occurred between 1230 and 1500 hours. During fMRI, participants completed a food perception task, similar to the task we have reported in previous papers.[16,25–27,29,32,33] Briefly, the food perception task consisted of a series of visual images of various food and non-food items. Images were presented in 30-second blocks that alternated between images of high-calorie (H) foods (for example, ice cream, cheeseburgers, cake, French fries, candy), low-calorie (L) foods (for example, fruits, vegetables, fresh salads, whole-grain bread and fresh fish) or control (C) images (that is, non-edible flowers, rocks and shrubs). Each block consisted of 10 images, each displayed for 3 s. A fixation cross (+) was displayed for 15 s at the beginning and end of the task to allow stabilization of the signal. The food perception task followed a constant presentation order (+, C, L, H, C, H, L, C, +) and lasted for a total duration of 240 s. Participants were asked to try to attend to the images in order to identify them in a later recognition test. After the scan, participants indicated their current level of hunger (that is, *Hunger*: 1 = not at all hungry; 7 = extremely hungry). Finally, participants were again shown all of the previously seen images and asked to rate 'how much you would like to eat each item right now' (that is, *Food Desire*: 1 = do not want to eat it; 7 = strongly desire to eat it).

Magnetic resonance imaging parameters

Neuroimaging was completed on a 3.0 Tesla SIEMENS Tim Trio scanner (Erlangen, Germany) using a 12-channel head coil. A T1-weighted 3D MPRAGE sequence (repetition time/echo time/flip angle = 2.1 s/2.25 ms/12°) was collected over 128 sagittal slices (256×256 matrix) with a slice thickness of 1.33 mm (voxel size = $1 \times 1 \times 1.33$ mm). For the 4-minute fMRI during the food perception task, a T2*-weighted echo-planar imaging sequence (repetition time/echo time/flip angle = 3.0 s/30 ms/90°) was collected over 43 transverse interleaved slices with 80 images per slice (3.5 mm thickness, no skip; 22.4 cm field of view; 64×64 acquisition matrix), with a voxel size of $3.5 \times 3.5 \times 3.5$ mm. The first 3 functional scans were discarded in order to achieve a steady-state equilibrium before data collection.

Image processing

Functional neuroimaging data were preprocessed and analyzed using SPM8 software (Wellcome Department of Cognitive Neurology, London, UK). Standard realignment and motion correction algorithms were employed to remove the effects of participant movement. The echo-planar images were coregistered to each individual's own T1 anatomical image, and spatially normalized to the template of the Montreal Neurological Institute. An isotropic Gaussian kernel (full width at half maximum = 6 mm) was used to spatially smooth the images, which were then resliced to $2 \times 2 \times 2$ mm. During preliminary statistical modeling, the time series was convolved with the canonical hemodynamic response function and a first-level autoregressive model was used to remove the effects of serial autocorrelation. Low frequency drift in the signal was removed by applying the default 128-second high pass filter.

Statistical analysis

The fMRI data were analyzed using a two-stage process. First, the various conditions (that is, high-calorie foods, low-calorie foods and control images) were each modeled against an implicit baseline and contrasts comparing the various conditions were constructed (for example, high-calorie versus low-calorie conditions). The high greater than low calorie contrast image for each subject was then used as the dependent variable in a second-level random effects multiple regression analysis. In this analysis, individual responses to the questions about *Appetite*, *Overeating*, *Hunger* and *Desire* were entered as separate predictor variables. The linear relation between each predictor variable and brain activation was examined separately while holding the effects of the other variables constant. Based on our *a priori* hypotheses, we restricted the primary analyses to six bilateral search territories (that is, bilateral amygdala, insula and medial orbitofrontal cortex) as defined by the Automated Anatomical Labeling Atlas,[34] implemented within the Wake Forest University SPM8 Toolbox PickAtlas Utility.[35] Activation maps for the regression analyses were initially thresholded at $P<0.001$, k (extent) $\geqslant 10$ contiguous voxels, and then subjected to small volume correction for multiple comparisons within each search territory at $P<0.05$, corrected for family-wise error. Finally, to determine the role of these activation regions in long-term responses to food, brain activation data were extracted from the entire activated cluster in each SPM analysis and entered simultaneously into a multiple linear regression analysis to predict BMI in SPSS 20. Based on prior evidence of sex differences in brain responses to food, we also evaluated this prediction separately for men and women. The multiple correlation coefficients from the separate regression models for men and women were compared directly using Fisher's r-to-z transform.

RESULTS

Scale intercorrelations

Scale intercorrelations among the various items are presented in Table 1. General *Appetite* was only significantly correlated with *Food Desire*. *Overeating* was significantly correlated with greater BMI and higher *Food Desire* ratings. State *Hunger* at the time of the scan was only related to *Food Desire* ratings of the images following the scan. Other associations were not significant. Together, these correlations provide preliminary evidence of the convergent and discriminant validity of the scales.

Appetite correlations

The relation between self-reported general *Appetite* ratings and brain responses to the high- versus low-calorie food perception condition was evaluated using multiple linear regression analysis. After statistically controlling for the influence of the other three variables in the regression (that is, *Overeating, Hunger and Food Desire*), *Appetite* was not significantly correlated with greater activation within any of the regions of interest to the high-calorie versus low-calorie food images (see Table 2). However, *Appetite* was associated with significantly reduced task-related activation of a cluster of voxels within the left amygdala (see Figure 1). Table 3 shows the R^2 for the overall model and individual β contributions of each of the predictor variables to the activation of this cluster. Figure 1 and Table 2 also show that *Appetite* was correlated with reduced activation of a cluster within the left posterior insula.

Overeating correlations

The relationship between self-reported *Overeating* and task-related brain responses was also evaluated. Holding other variables constant (*Appetite, Hunger and Food Desire*), self-reported *Overeating* was associated with increased responsiveness to the high-calorie food condition for an activation cluster located within the right medial orbitofrontal gyrus (see Table 2 and Figure 1). In contrast, there were no negative correlations between *Overeating* and task-related brain responses within any of the search regions.

Hunger correlations

Hunger ratings taken immediately after the scan were also examined independently in the regression. After controlling for the other variables (that is, *Appetite, Overeating and Food Desire*), self-rated *Hunger* was positively correlated with activation within a small cluster of the right amygdala (see Table 2 and Figure 1). There were no activation clusters showing a negative correlation between *Hunger* and task-related brain activation within the regions of interest.

Food desire correlations

Actual ratings of the food images obtained immediately after the scan were also examined for their independent contribution to brain responses for the high- versus low-calorie foods. With the other variables (that is, *Appetite, Overeating and Hunger*) statistically controlled, *Food Desire* was positively correlated with activation within a small cluster within the left amygdala (see Table 2 and Figure 1), but no clusters showed any negative correlation with *Food Desire* during the task.

Exploratory whole-brain analyses

To aid in generation of future hypotheses, each of the preceding regression analyses were also examined at the whole-brain level (that is, not constrained to the hypothesized regions of interest). However, no regions of activation survived whole brain (family-wise error $P<0.05$) correction for multiple comparisons within any of the analyses.

Table 1. Intercorrelations among primary food motivation questions

Scale	*1*	*2*	*3*	*4*	*5*
1. BMI	—	−0.214	0.335*	−0.204	−0.086
2. Appetite		—	0.230	0.293	0.517**
3. Overeating			—	0.067	0.524**
4. Hunger				—	0.519**
5. Food desire					—

Abbreviation: BMI, body mass index. *$P<0.05$, **$P\leqslant0.001$

Table 2. Locations of maximally activated voxels during multiple regression analysis

Comparison region	*Cluster size (voxels)*	*x*	*y*	*z*	*SPM {t}*
Appetite					
Positive					
No active voxels	—	—	—	—	—
Negative					
Left amygdala	11	−16	−2	−14	4.09
Left insula	26	−40	−8	8	4.77
Overeat					
Positive					
R medial orbitofrontal gyrus	16	8	34	−14	4.14
Negative					
No active voxels	—	—	—	—	—
Hunger					
Positive					
Right amygdala	3	18	−2	−14	4.11
Negative					
No active voxels	—	—	—	—	—
Food desire ratings					
Positive					
Left amygdala	9	−18	−4	−16	4.62
Negative					
No active voxels	—	—	—	—	—

Abbreviation: SPM, statistical parametric map.

Multiple regression to predict BMI

The final goal was to determine whether the combined brain activation clusters identified in the preceding analyses could be used to predict an independently obtained indicator of an individual's long-term eating behavior; in this case we attempted to predict BMI from these cluster responses. For each of the five activation clusters identified in the previous analyses, the cluster eigenvariate was extracted and entered as a predictor variable in a multiple regression analysis with BMI as the dependent variable. Standard regression diagnostics were undertaken to identify particularly influential observations that may have affected the analyses. No participants scored more than 3 s.d. from the mean BMI score and no cases showed excessive influence on the regression analysis (that is, high leverage values or Cook's Distance scores). For the sample as a whole, a model including all five

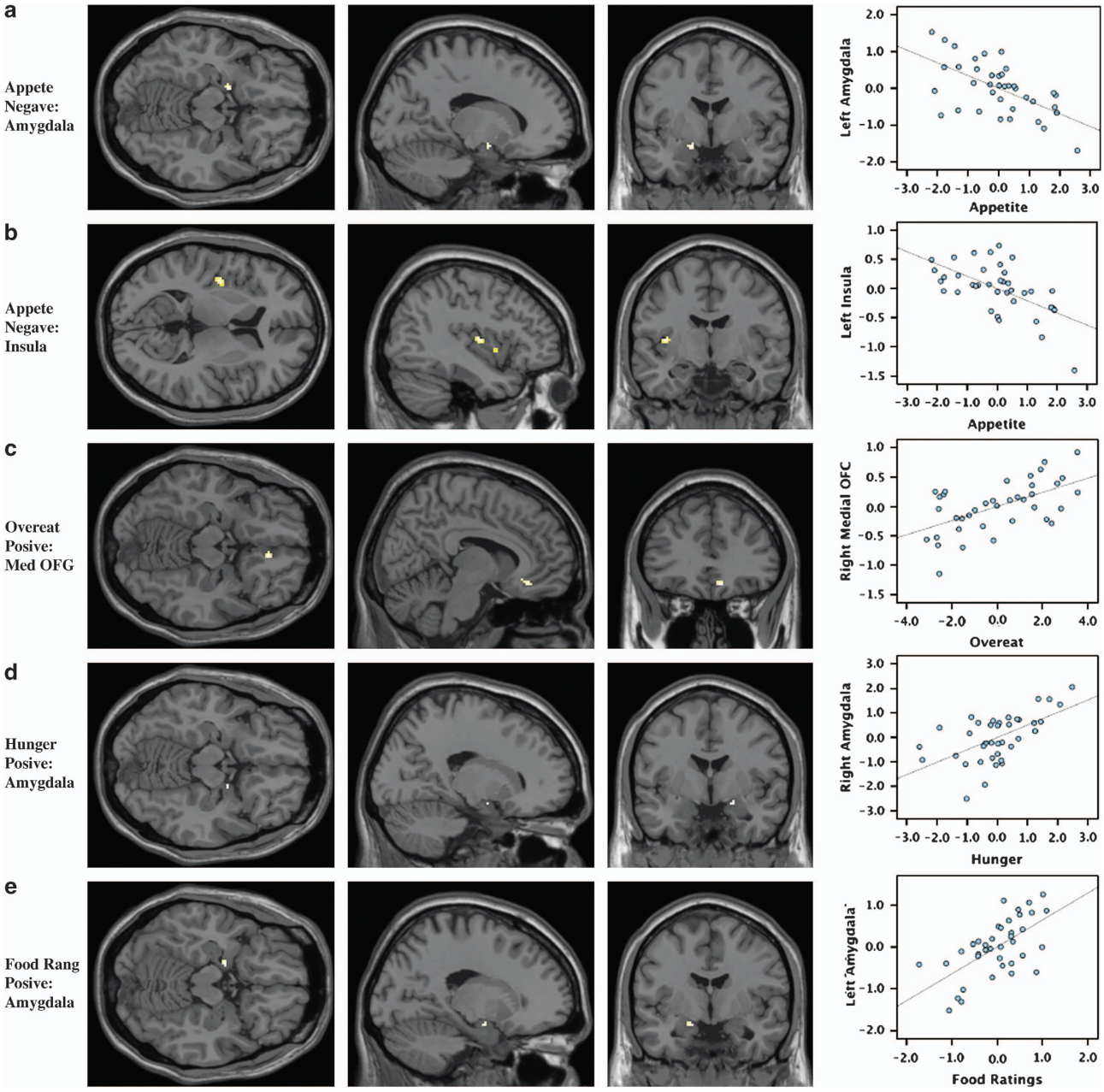


Figure 1. The figure depicts the results of the primary regression analyses for each of the four food motivation scales on brain responses to the high-calorie > low-calorie food contrast, while holding the other three scales constant. The first three columns show the locus of the primary cluster of activation revealed in the regression, and the right hand column depicts the partial correlation scatterplot between the food motivation variable and cluster signal intensity for the data in the highlighted cluster. The figure shows that general Appetite was negatively correlated with clusters in the (**a**) left amygdala and (**b**) left insula. Overeating was associated with greater responsiveness within (**c**) the right medial orbitofrontal cortex (OFC). Hunger ratings were positively correlated with a cluster in the (**d**) right amygdala, while Food Desirability ratings were positively correlated with a cluster in the (**e**) left amygdala.

activation clusters as predictors did not significantly predict BMI, $R^2 = 0.166$, $P = 0.30$. However, when the same model was tested separately by sex, we found striking differences in model prediction. Whereas there was no significant relation between combined activation from the extracted regions and BMI, $R^2 = 0.138$, $P = 0.76$ for males, activation within these same regions was highly predictive of BMI for females, $R^2 = 0.756$, $P = 0.007$. To directly compare the variance explained by these two models, we used a Fisher's r-to-z transformation of the two multiple correlation coefficients and compared the resulting difference using the z-distribution. This comparison was significant ($z = 2.62$, $P = 0.009$), suggesting that the combined activation from the five brain regions was significantly more predictive of BMI for males than for females. The results were virtually unchanged when menstrual phase was statistically controlled as a nuisance covariate. These findings suggest that long-term weight status among females is closely related to the responsiveness of these brain regions to images of calorie-rich foods. Figure 2 presents the partial correlation plots showing the association between BMI and the standardized predicted scores from the combined activation clusters for males and females.

Table 3. Multiple regression analyses predicting extracted brain responses from food motivation

Predictor region	*β*	*t*	*Significance*
Appetite predicts left amygdala (Model $R^2 = 0.476$)			
Appetite	−0.625	−4.241	0.0002
Overeat	−0.138	−0.892	0.379
Hunger	0.159	1.036	0.308
Desire	0.714	3.637	0.001
Appetite predicts left insula (model $R^2 = 0.371$)			
Appetite	−0.685	−4.240	0.0002
Overeat	0.111	0.655	0.517
Hunger	0.065	0.387	0.701
Desire	0.142	0.661	0.513
Overeating predicts right medial orbitofrontal gyrus ($R^2 = 0.332$)			
Appetite	−0.053	0.321	0.750
Overeat	0.696	3.994	0.0003
Hunger	0.147	0.845	0.404
Desire	−0.456	−2.055	0.048
Hunger predicts right amygdala ($R^2 = 0.352$)			
Appetite	−0.172	−1.049	0.302
Overeat	0.173	1.009	0.320
Hunger	0.703	4.114	0.0002
Desire	−0.382	−1.751	0.089
Food desire predicts left amygdala ($R^2 = 0.444$)			
Appetite	−0.506	−3.528	0.001
Overeat	−0.169	−1.124	0.269
Hunger	0.053	0.354	0.726
Desire	0.869	4.548	0.0001

DISCUSSION

We examined the covariation between regional brain responses to food images and several components of food motivation that might contribute to weight gain and obesity, including general appetite ratings, overeating propensity, current hunger status and ratings of food desirability. These motivational variables were each related to activation within several regions hypothesized a priori to be central in regulating food intake, including the amygdala, posterior insula and medial orbitofrontal cortex. These regions were selected based on prior evidence of their role in processing of visual images of food[25–29] and regulating food intake,[30,31] but likely reflect only a subset of potential brain regions that may be involved. Overall, within this limited set of regions of interest, we found that those who reported greater general appetite tended to show reduced activation within the left amygdala and posterior left insula to images of high- relative to low-calorie foods, while those reporting a tendency to overeat showed greater responsiveness within the medial orbitofrontal cortex to such images. Greater self-rated hunger at the time of the scan was associated with increased responsiveness of voxels within the right amygdala to the high-calorie images, while greater desire to eat the foods depicted was associated with increased activation within the left amygdala. These regions together appear to be reliably responsive to food imagery and correlate significantly with several behaviorally relevant dimensions of eating behavior that may contribute to unhealthy weight gain. Moreover, when the activation within these regions was combined to predict a global measure of long-term food consumption (that is, BMI), there were clear distinctions between men and women in the relation between these brain responses and weight status. Whereas brain responses within these specific food-responsive regions were essentially unrelated to BMI for males, combined activation in these same regions accounted for 76% of the variance in body mass among females. These findings suggest that motivational processing of food images within the brain regions studied here may be reliably related to weight status among women, but may be less so among men.

Several important findings emerge from this study. First, we confirm that specific aspects of food motivation are related to the responsiveness of a core set of brain regions that have been implicated in prior studies of visual food imagery.[36] General appetite, which reflects an individual's self-reported persistent desire for food across settings, was inversely correlated with left amygdala and insular responses to images of high-calorie foods, such that greater responses within these regions were associated with lower appetite ratings. The amygdala has long been implicated in studies of appetitive behavior and food motivation,[37] and lesions to the amygdala often result in severe changes in food seeking and consumption.[38,39] In a prior study, appetite ratings were suppressed following a 6-week regimen of daily citicoline administration, and the magnitude of appetite decline was inversely correlated with amygdala and insular responses to images of high-calorie foods,[29] suggesting that these structures may have a role in appetite for food. The present findings are also consistent with the hypothesized role of the amygdala in detecting and responding to potential threat or harmful stimuli in the environment,[40,41] and the role of the insula in internally generated sensations of disgust.[42,43] The insula is believed to be part of the extended gustatory cortex and a key region involved in visceral sensation and interoceptive awareness.[44] Activation of this region occurs in response to satiety,[45] perception of painful and disgusting stimuli,[46] and with greater sensitivity to the visceral somatic sensations associated with anxiety.[47] This may be important for general appetite, as individuals with greater disgust sensitivity tend to be more restrained in their eating.[48] When considered in light of existing research on these brain regions, we speculate that the present finding suggest that individuals with a lower general appetite might have a broad propensity to perceive calorie-rich foods as less appealing, more aversive or even potentially threatening, leading to increased amygdala and insular responses to such stimuli. Of course, the causal direction of this association cannot be inferred from these cross-sectional data, so it remains to be determined whether reduced appetite leads to increased amygdala and insula responses to food, or whether the activation of these regions contributes causally to a decreased desire for food.

Regardless of general appetite, some individuals are particularly prone to eat more than they intend when snacking or consuming a meal. In response to images of calorie-rich foods, self-reported overeating was uniquely associated with increased activation within the medial orbitofrontal cortex, a region that is consistently implicated in reward processes and food preferences.[49,50] For example, in one compelling study, participants underwent positron emission tomography scanning while eating pieces of chocolate to the point of satiety.[51] Early in the scan, when the chocolate was still perceived as highly pleasurable, elevated brain activity was found within the caudal regions of the medial orbitofrontal cortex, proximal to the region activated here, but as participants continued to consume additional pieces of chocolate to the point of repulsion, this activation diminished and was replaced by activation within the lateral prefrontal cortex.[51] A number of studies have now suggested that the medial orbitofrontal cortex directly tracks the subjective pleasantness of stimuli,[52] and this region may contribute directly to decision-making processes that involve pleasure and reward.[53] Higher scores on a food addiction scale also correlated with greater activation within the medial orbitofrontal cortex when anticipating the receipt of highly palatable food,[54] and this region is also more responsive to food images following a fasting relative to a satiated state.[55] In fact, some studies have pointed to

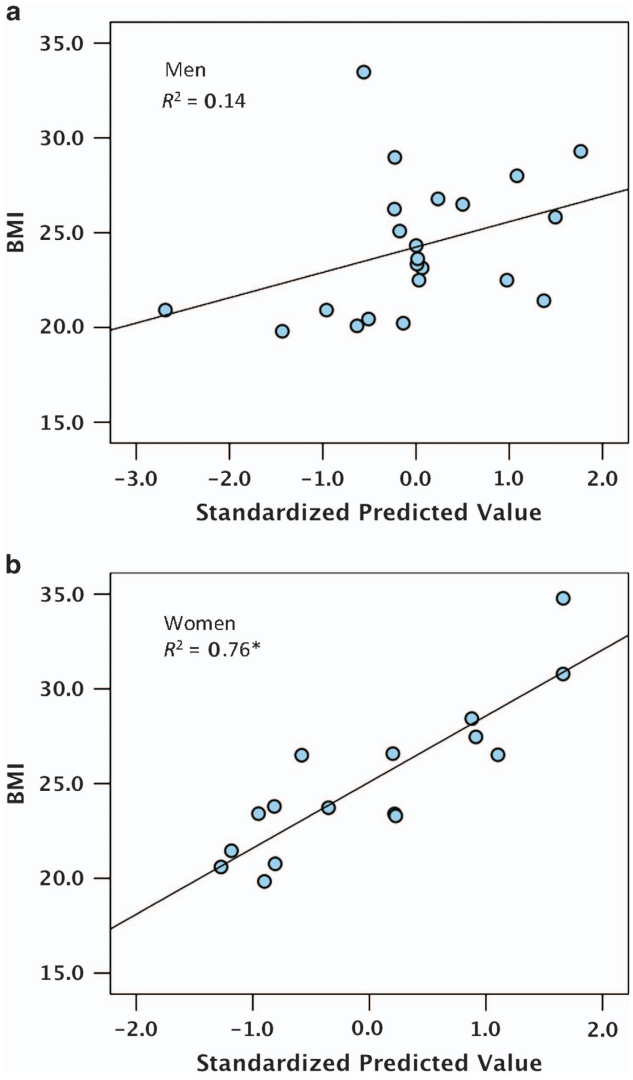


Figure 2. The figure depicts the partial correlation plots from the secondary regression analyses. In this analysis, the combined brain responses extracted from the primary analyses were used to predict BMI scores separately for men and women. Whereas the extracted functional clusters were not related to BMI among men, they were highly significantly related for women ($R^2 = 0.76$, $^*P = 0.007$).

an association between altered functioning[32,56] or structure[57] of the medial orbitofrontal cortex and general weight status. Greater responsiveness of the medial orbitofrontal cortex to high-calorie food cues may reflect a hyper-sensitivity to the reward value of such foods,[54,58] and might even serve as a risk factor for obesity. Future research may explore whether the responsiveness of this region to rewarding food stimuli may be predictive of long-term weight gain.

We also examined acute hunger at the time of the scan and found that it correlated positively with activation within the right amygdala during perception of the high- versus low-calorie food images, after controlling for other motivational variables. The present findings corroborate prior work showing that acute hunger is a powerful modulator of amygdala responses to images of food.[18,20,30,55] For instance, significantly greater right amygdala activation was found in response to food images during a hungry state (that is, 14 h fasting) compared with satiation (that is, an hour after ingesting pizza *ad libitum*).[59] A recent meta-analysis supported the modulating effect of hunger on right amygdala responses to food pictures.[36] These findings are also consistent with other research suggesting that the amygdala has an important role in determining the motivational salience of a stimulus,[60] and suggest that this salience detection system may be influenced by the motivational status of the individual. Similarly, after controlling for global appetite, overeating and hunger, we also found that the strength of desire to eat the foods depicted in the images was associated with greater response magnitude within the left amygdala to the high- versus low-calorie foods. It is particularly interesting to note that a cluster within the left amygdala was positively correlated with actual ratings of food desirability while a nearby cluster of activation was negatively correlated with general appetite, as described earlier. Although the resolution of our data precludes precise localization within the amygdala, we did find that the cluster associated with ratings of greater food desirability was located slightly more posteriorly than that associated with lower general appetite. Both clusters were collocated within an area corresponding to the superficial and centromedial nucleus groups,[61] which project extensively to the orbitofrontal cortex[62] and are broadly implicated in generating autonomic, behavioral and emotional signals based on prior learning.[63]

The primary goal of the present study was to determine the degree to which the identified food-responsive brain activation patterns might relate to long-term weight status among men and women. We found that motivation-related responses to the calorie-rich food images were highly predictive of BMI for women, accounting for up to 76% of variance in weight status, but these same regional brain responses were essentially unrelated to body mass among men. These findings raise the possibility that different factors may contribute to body weight composition for men and women. For women, body mass appears to be significantly related to specific cortico-limbic responses when confronted with visual food cues, particularly images of foods high in calorie density. On the other hand, such an association between brain responses to visual food cues and BMI was essentially absent for men, suggesting that body mass among men is likely to be more affected by any of a number of other factors that were not examined in the current study. The present findings build upon prior work showing that women tend to show greater cortico-limbic responses to visual images of high-calorie food compared with men,[16,64] and further suggest that long-term body weight status in women may be associated with greater responsiveness of the food motivation network to visual images depicting highly palatable food. Although further research will be necessary to determine the extent to which these findings may relate to actual food consumption and weight gain, these preliminary findings may have important implications regarding the higher rates of obesity[2,4] and eating disorders[5–7] among women. In light of these findings, future interventions may benefit by focusing on developing methods to circumvent the neurobehavioral links between visual responses to food and eventual food consumption. Even simple awareness of the possibility that women may be particularly responsive to visual cues of food stimuli may serve as a potential method for curtailing food intake by overtly restricting exposure to such cues.

Several limitations should be borne in mind when interpreting these findings. First, we only explored self-reported food motivation, including self-ratings of general appetite, overeating, hunger and food preferences. As self-reported motivation may differ from actual behavior, it will be important to corroborate these findings using experimental techniques that involve measuring objective eating behavior. Second, participants were screened to exclude psychopathology, and no attempts were made to recruit based on weight status, so the findings may have limited generalizability to patients with eating disorders or those at the extremes of the weight continuum. Third, with the exception of preventing food intake for an hour prior to the scan, we did not directly manipulate hunger status or total calorie

intake. This permitted us to measure brain responses across a normal spectrum of hunger and satiety, but may have also introduced error variance that potentially reduced our power to detect some statistical effects. Future research may benefit from direct manipulation of hunger status by holding calorie intake constant for a longer interval before the scan. Fourth, although we found significant differences between men and women in the relationship between regional brain responses and BMI, we cannot exclude the possibility that the findings were driven by other factors that were not examined or controlled in the current study. It is conceivable that body mass among men may be better accounted for by some other combination of elementary biological or physiological factors such as serum testosterone, age-related somatic changes, activity level or even to social or gender-role variables that influence the circumstances surrounding food and beverage consumption in western cultures. It is also possible that the present sex difference emerged because of the greater variation in lean muscle mass as a component of BMI among men versus women[65] or even that men were simply less reliable at reporting height and weight than women. Future work should examine other more direct indices of fat to lean muscle mass to verify the currently observed sex differences. Finally, our primary hypotheses only focused on a small number of discrete brain regions. Although whole-brain analyses failed to show additional regions of correlation following stringent corrections for multiple comparisons, it is likely that at less stringent thresholds, other critically important regions may also emerge as significant. Thus, we make no claims that the regions observed here are the only ones that may be important in this process. Future work examining other regions important for food processing may also enhance our understanding of the neural underpinnings leading to weight gain and obesity. Despite these limitations, the present findings provide further support for a key network of regions involved in food motivation and further suggest that the responses within this network during visual perception of high-calorie foods are directly and strongly related to long-term weight status among women. These findings raise the speculative possibility that the vulnerabilities to weight gain, obesity and eating disorders, which predominate among women may be influenced to some extent by a greater neurocognitive responsiveness to the visual cues associated with food images.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ACKNOWLEDGEMENTS

This research was supported by a USAMRAA grant (W81XWH-09-1-0730).

REFERENCES

1 Flegal KM, Carroll MD, Ogden CL, Johnson CL. Prevalence and trends in obesity among US adults, 1999-2000. *JAMA* 2002; **288**: 1723–1727.
2 Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of obesity in the United States, 2009-2010. *NCHS Data Brief* 2012; **82**: 1–8.
3 Overweight, obesity, and health risk. National task force on the prevention and treatment of obesity. *Arch Intern Med* 2000; **160**: 898–904.
4 Ogden CL, Carroll MD, Curtin LR, McDowell MA, Tabak CJ, Flegal KM. Prevalence of overweight and obesity in the United States, 1999-2004. *JAMA* 2006; **295**: 1549–1555.
5 Lewinsohn PM, Seeley JR, Moerk KC, Striegel-Moore RH. Gender differences in eating disorder symptoms in young adults. *Int J Eat Disord* 2002; **32**: 426–440.
6 Striegel-Moore RH, Bulik CM. Risk factors for eating disorders. *Am Psychol* 2007; **62**: 181–198.
7 Striegel-Moore RH, Rosselli F, Perrin N, DeBar L, Wilson GT, May A *et al.* Gender difference in the prevalence of eating disorder symptoms. *Int J Eat Disord* 2009; **42**: 471–474.
8 Yeo GS, Heisler LK. Unraveling the brain regulation of appetite: lessons from genetics. *Nat Neurosci* 2012; **15**: 1343–1349.
9 Zeltser LM, Seeley RJ, Tschop MH. Synaptic plasticity in neuronal circuits regulating energy balance. *Nat Neurosci* 2012; **15**: 1336–1342.
10 Williams KW, Elmquist JK. From neuroanatomy to behavior: central integration of peripheral signals regulating feeding behavior. *Nat Neurosci* 2012; **15**: 1350–1355.
11 Gregersen NT, Moller BK, Raben A, Kristensen ST, Holm L, Flint A *et al.* Determinants of appetite ratings: the role of age, gender, BMI, physical activity, smoking habits, and diet/weight concern. *Food Nutr Res* 2011; **55**: doi: 10.3402/fnr.v55i0.7028.
12 Hooper N, Sandoz EK, Ashton J, Clarke A, McHugh L. Comparing thought suppression and acceptance as coping techniques for food cravings. *Eat Behav* 2012; **13**: 62–64.
13 Moore CJ, Cunningham SA. Social position, psychological stress, and obesity: a systematic review. *J Acad Nutr Diet* 2012; **112**: 518–526.
14 Verstuyf J, Patrick H, Vansteenkiste M, Teixeira PJ. Motivational dynamics of eating regulation: a self-determination theory perspective. *Int J Behav Nutr Phys Act* 2012; **9**: 21.
15 Cornier MA, Salzberg AK, Endly DC, Bessesen DH, Tregellas JR. Sex-based differences in the behavioral and neuronal responses to food. *Physiol Behav* 2010; **99**: 538–543.
16 Killgore WDS, Yurgelun-Todd DA. Sex differences in cerebral responses to images of high versus low-calorie food. *Neuroreport* 2010; **21**: 354–358.
17 Lawrence NS, Hinton EC, Parkinson JA, Lawrence AD. Nucleus accumbens response to food cues predicts subsequent snack consumption in women and increased body mass index in those with reduced self-control. *Neuroimage* 2012; **63**: 415–422.
18 LaBar KS, Gitelman DR, Parrish TB, Kim YH, Nobre AC, Mesulam MM. Hunger selectively modulates corticolimbic activation to food stimuli in humans. *Behav Neurosci* 2001; **115**: 493–500.
19 Lutter M, Nestler EJ. Homeostatic and hedonic signals interact in the regulation of food intake. *J Nutr* 2009; **139**: 629–632.
20 Piech RM, Lewis J, Parkinson CH, Owen AM, Roberts AC, Downing PE *et al.* Neural correlates of appetite and hunger-related evaluative judgments. *PLoS One* 2009; **4**: e6581.
21 Nederkoorn C, Houben K, Hofmann W, Roefs A, Jansen A. Control yourself or just eat what you like? Weight gain over a year is predicted by an interactive effect of response inhibition and implicit preference for snack foods. *Health Psychol* 2010; **29**: 389–393.
22 Hofmann W, Friese M, Roefs A. Three ways to resist temptation: the independent contributions of executive attention, inhibitory control, and affect regulation to the impulse control of eating behavior. *J Exp Soc Psychol* 2009; **45**: 431–435.
23 Batterink L, Yokum S, Stice E. Body mass correlates inversely with inhibitory control in response to food among adolescent girls: an fMRI study. *Neuroimage* 2010; **52**: 1696–1703.
24 Gruber AJ, McDonald RJ. Context, emotion, and the strategic pursuit of goals: interactions among multiple brain systems controlling motivated behavior. *Front Behav Neurosci* 2012; **6**: 50.
25 Killgore WDS, Young AD, Femia LA, Bogorodzki P, Rogowska J, Yurgelun-Todd DA. Cortical and limbic activation during viewing of high- versus low-calorie foods. *Neuroimage* 2003; **19**: 1381–1394.
26 Killgore WDS, Yurgelun-Todd DA. Developmental changes in the functional brain responses of adolescents to images of high and low-calorie foods. *Dev Psychobiol* 2005; **47**: 377–397.
27 Killgore WDS, Yurgelun-Todd DA. Positive affect modulates activity in the visual cortex to images of high calorie foods. *Int J Neurosci* 2007; **117**: 643–653.
28 Siep N, Roefs A, Roebroeck A, Havermans R, Bonte ML, Jansen A. Hunger is the best spice: an fMRI study of the effects of attention, hunger and calorie content on food reward processing in the amygdala and orbitofrontal cortex. *Behav Brain Res* 2009; **198**: 149–158.
29 Killgore WDS, Ross AJ, Kamiya T, Kawada Y, Renshaw PF, Yurgelun-Todd DA. Citicoline affects appetite and cortico-limbic responses to images of high-calorie foods. *Int J Eat Disord* 2010; **43**: 6–13.
30 Mehta S, Melhorn SJ, Smeraglio A, Tyagi V, Grabowski T, Schwartz MW *et al.* Regional brain response to visual food cues is a marker of satiety that predicts food choice. *Am J Clin Nutr* 2012; **96**: 989–999.
31 Murdaugh DL, Cox JE, Cook 3rd EW, Weller RE. fMRI reactivity to high-calorie food pictures predicts short- and long-term outcome in a weight-loss program. *Neuroimage* 2012; **59**: 2709–2721.
32 Killgore WDS, Yurgelun-Todd DA. Body mass predicts orbitofrontal activity during visual presentations of high-calorie foods. *Neuroreport* 2005; **16**: 859–863.
33 Killgore WDS, Yurgelun-Todd DA. Affect modulates appetite-related brain activity to images of food. *Int J Eat Disord* 2006; **39**: 357–363.
34 Tzourio-Mazoyer N, Landeau B, Papathanassiou D, Crivello F, Etard O, Delcroix N *et al.* Automated anatomical labeling of activations in SPM using a

macroscopic anatomical parcellation of the MNI MRI single-subject brain. *Neuroimage* 2002; **15**: 273–289.
35 Maldjian JA, Laurienti PJ, Kraft RA, Burdette JH. An automated method for neuroanatomic and cytoarchitectonic atlas-based interrogation of fMRI data sets. *Neuroimage* 2003; **19**: 1233–1239.
36 van der Laan LN, de Ridder DT, Viergever MA, Smeets PA. The first taste is always with the eyes: a meta-analysis on the neural correlates of processing visual food cues. *Neuroimage* 2011; **55**: 296–303.
37 Goddard GV. Functions of the Amygdala. *Psychol Bull* 1964; **62**: 89–109.
38 Loscher W, Brandt C, Ebert U. Excessive weight gain in rats over extended kindling of the basolateral amygdala. *Neuroreport* 2003; **14**: 1829–1832.
39 Malkova L, Mishkin M, Suomi SJ, Bachevalier J. Long-term effects of neonatal medial temporal ablations on socioemotional behavior in monkeys (Macaca mulatta). *Behav Neurosci* 2010; **124**: 742–760.
40 Eippert F, Veit R, Weiskopf N, Erb M, Birbaumer N, Anders S. Regulation of emotional responses elicited by threat-related stimuli. *Hum Brain Mapp* 2007; **28**: 409–423.
41 Phelps EA, O'Connor KJ, Gatenby JC, Gore JC, Grillon C, Davis M. Activation of the left amygdala to a cognitive representation of fear. *Nat Neurosci* 2001; **4**: 437–441.
42 Britton JC, Phan KL, Taylor SF, Welsh RC, Berridge KC, Liberzon I. Neural correlates of social and nonsocial emotions: an fMRI study. *Neuroimage* 2006; **31**: 397–409.
43 Fitzgerald DA, Posse S, Moore GJ, Tancer ME, Nathan PJ, Phan KL. Neural correlates of internally-generated disgust via autobiographical recall: a functional magnetic resonance imaging investigation. *Neurosci Lett* 2004; **370**: 91–96.
44 Augustine JR. Circuitry and functional aspects of the insular lobe in primates including humans. *Brain Res* 1996; **22**: 229–244.
45 Morris JS, Dolan RJ. Involvement of human amygdala and orbitofrontal cortex in hunger-enhanced memory for food stimuli. *J Neurosci* 2001; **21**: 5304–5310.
46 Benuzzi F, Lui F, Duzzi D, Nichelli PF, Porro CA. Does it look painful or disgusting? Ask your parietal and cingulate cortex. *J Neurosci* 2008; **28**: 923–931.
47 Killgore WDS, Britton JC, Price LM, Gold AL, Deckersbach T, Rauch SL. Neural correlates of anxiety sensitivity during masked presentation of affective faces. *Depress Anxiety* 2011; **28**: 243–249.
48 Houben K, Havermans RC. A delicious fly in the soup. The relationship between disgust, obesity, and restraint. *Appetite* 2012; **58**: 827–830.
49 Kringelbach ML, Rolls ET. The functional neuroanatomy of the human orbitofrontal cortex: evidence from neuroimaging and neuropsychology. *Prog Neurobiol* 2004; **72**: 341–372.
50 Rolls ET. The orbitofrontal cortex and reward. *Cereb Cortex* 2000; **10**: 284–294.
51 Small DM, Zatorre RJ, Dagher A, Evans AC, Jones-Gotman M. Changes in brain activity related to eating chocolate: from pleasure to aversion. *Brain* 2001; **124**(Pt 9): 1720–1733.
52 Grabenhorst F, Rolls ET. Different representations of relative and absolute subjective value in the human brain. *Neuroimage* 2009; **48**: 258–268.
53 Grabenhorst F, Rolls ET. Value, pleasure and choice in the ventral prefrontal cortex. *Trends Cogn Sci* 2011; **15**: 56–67.
54 Gearhardt AN, Yokum S, Orr PT, Stice E, Corbin WR, Brownell KD. Neural correlates of food addiction. *Arch Gen Psychiat* 2011; **68**: 808–816.
55 Holsen LM, Zarcone JR, Thompson TI, Brooks WM, Anderson MF, Ahluwalia JS *et al.* Neural mechanisms underlying food motivation in children and adolescents. *Neuroimage* 2005; **27**: 669–676.
56 Volkow ND, Wang GJ, Telang F, Fowler JS, Thanos PK, Logan J *et al.* Low dopamine striatal D2 receptors are associated with prefrontal metabolism in obese subjects: possible contributing factors. *Neuroimage* 2008; **42**: 1537–1543.
57 Smucny J, Cornier MA, Eichman LC, Thomas EA, Bechtell JL, Tregellas JR. Brain structure predicts risk for obesity. *Appetite* 2012; **59**: 859.
58 Nolan-Poupart S, Veldhuizen MG, Geha P, Small DM. Midbrain response to milkshake correlates with ad libitum milkshake intake in the absence of hunger. *Appetite* 2013; **60**: 168–174.
59 Fuhrer D, Zysset S, Stumvoll M. Brain activity in hunger and satiety: an exploratory visually stimulated FMRI study. *Obesity (Silver Spring)* 2008; **16**: 945–950.
60 Santos A, Mier D, Kirsch P, Meyer-Lindenberg A. Evidence for a general face salience signal in human amygdala. *Neuroimage* 2011; **54**: 3111–3116.
61 Kim HJ, Kim N, Kim S, Hong S, Park K, Lim S *et al.* Sex differences in amygdala subregions: evidence from subregional shape analysis. *Neuroimage* 2012; **60**: 2054–2061.
62 Bach DR, Behrens TE, Garrido L, Weiskopf N, Dolan RJ. Deep and superficial amygdala nuclei projections revealed in vivo by probabilistic tractography. *J Neurosci* 2011; **31**: 618–623.
63 LeDoux JE. Emotion circuits in the brain. *Annu Rev Neurosci* 2000; **23**: 155–184.
64 Frank S, Laharnar N, Kullmann S, Veit R, Canova C, Hegner YL *et al.* Processing of food pictures: influence of hunger, gender and calorie content. *Brain Res* 2010; **1350**: 159–166.
65 Gallagher D, Visser M, Sepulveda D, Pierson RN, Harris T, Heymsfield SB. How useful is body mass index for comparison of body fatness across age, sex, and ethnic groups? *Am J Epidemiol* 1996; **143**: 228–239.

Insomnia-related complaints correlate with functional connectivity between sensory–motor regions

William D.S. Killgore[a,b], Zachary J. Schwab[a], Maia Kipman[a], Sophie R. DelDonno[a] and Mareen Weber[a,b]

According to the hyperarousal theory of insomnia, difficulty in initiating or maintaining sleep occurs as a result of increased cognitive and physiological arousal caused by acute stressors and associated cognitive rumination, placing the individual in a perpetual cycle of hyperarousal and increased sensitivity to sensory stimulation. We tested the hypothesis that difficulty in initiating or maintaining sleep would be associated with increased functional connectivity between primary sensory processing and motor planning regions. Fifty-eight healthy adults (29 men, 29 women) completed a self-report inventory about sleep onset and maintenance problems and underwent a 6-min resting-state functional MRI scan. Bilateral regions of interest (ROIs) were placed in primary visual cortex, auditory cortex, olfactory cortex, and the supplementary motor cortex, and the mean processed signal time course was extracted and correlated with each of the other ROIs. Difficulty in falling asleep was associated with increased functional connectivity between the primary visual cortex and other sensory regions such as the primary auditory cortex, olfactory cortex, and the supplementary motor cortex. The primary auditory cortex also showed greater connectivity with the supplementary motor cortex in those with sleep initiation problems. Problems with sleep maintenance were associated with greater connectivity between the primary visual cortex and the olfactory cortex. Consistent with the predictions of the hyperarousal model, difficulty in falling asleep was associated with greater functional connectivity between primary sensory and supplementary motor regions. Such augmented functional connectivity may contribute to the sustained sensory processing of environmental stimuli, potentially prolonging the latency to sleep. *NeuroReport* 24:233–240 © 2013 Wolters Kluwer Health | Lippincott Williams & Wilkins.

NeuroReport 2013, **24**:233–240

Keywords: connectivity, functional MRI, insomnia, sensory cortices, sleep initiation dysfunction, sleep maintenance

[a]Center for Depression, Anxiety, and Stress Research, McLean Hospital, Belmont and [b]Department of Psychiatry, Harvard Medical School, Boston, Massachusetts, USA

Correspondence to William D.S. Killgore, PhD, Center for Depression, Anxiety, and Stress Research, McLean Hospital, Harvard Medical School, 115 Mill Street, Belmont, MA 02478, USA
Tel: +1 617 855 3166; fax: +1 617 855 2770;
e-mail: killgore@mclean.harvard.edu

Received 11 December 2012 **accepted** 9 January 2013

Introduction

Insomnia can be defined as a condition involving difficulty in obtaining sufficient restorative sleep either because of excessive latency to fall asleep, difficulty in remaining asleep, or poor quality sleep that leads to notable impairment in daytime functioning [1]. Formal diagnosis requires symptoms to be present for 4 weeks or longer, and depending on the classification scheme, insomnia can be designated as primary insomnia (PI), insomnia related to a medical or psychiatric condition, or insomnia due to the influence of a substance [2]. Whereas the diagnostic prevalence of PI in the general population is between 3 and 5% [3], close to half of the population experience some symptoms of insomnia that may not necessarily be associated with a formal diagnosis [1]. Over one-third of the population reports symptoms of insomnia, including difficulty in initiating sleep, maintaining sleep, or obtaining nonrestorative sleep at least three times per week [4].

The hyperarousal theory of insomnia posits that difficulty in initiating or maintaining sleep occurs as a result of increased cognitive and physiological arousal caused by acute stressors and associated cognitive rumination [5]. As the latency to sleep is prolonged and rumination continues, the individual becomes even more emotionally aroused because of concerns over his/her inability to sleep and its potential consequences, resulting in a vicious cycle that escalates somatic and cortical hyperarousal, leading to further difficulty in sleeping. Compared with healthy sleepers, individuals with PI show greater high-frequency electroencephalographic activity (EEG) in the β range (14–35 Hz) around the time that they are falling asleep [6]. Increased β power has also been observed during stage 2 nonrapid eye movement (NREM) sleep in PI [7]. Some evidence suggests that this hyperaroused EEG pattern may be persistent even during normal waking [8], indicative of a chronic state of hyperarousal throughout the day. Because this pattern of EEG activity is believed to be fundamental to cognitive and sensory processing, a core feature of the hyperarousal theory of insomnia involves increased sensory processing that interferes with the onset and maintenance of sleep [1]. Thus, individuals with insomnia find themselves in a perpetual cycle of hyperarousal and increased sensitivity to sensory stimulation, which leads to further cortical arousal and difficulty in sleep initiation and maintenance.

0959-4965 © 2013 Wolters Kluwer Health | Lippincott Williams & Wilkins DOI: 10.1097/WNR.0b013e32835edbdd

On the basis of the hyperarousal theory of insomnia, we hypothesized that heightened sensory processing would be evident in the form of increased resting-state functional connectivity between sensory regions and motor preparatory regions of the cortex among individuals reporting problems in initiating and/or maintaining sleep. We therefore expected that daytime functional connectivity among sensory–motor regions would be related to difficulty in falling asleep at night among those with insomnia. Healthy normal participants completed a questionnaire about their sleep problems and underwent a 6-min resting-state functional connectivity scan. Individuals reporting difficulty in falling asleep or remaining asleep were hypothesized to show greater functional connectivity between the primary visual cortex, primary auditory cortex, olfactory cortex, and the supplementary motor cortex compared with those without such complaints.

Methods

Participants

Fifty-eight healthy adults (50% women) between 18 and 45 years of age (mean = 30.5; SD = 8.0) participated in the study. A thorough telephone screening was conducted to rule out medical, neurological, or psychiatric problems, including excessive substance use or abuse. All participants provided written informed consent and were compensated for their time. This research protocol was reviewed and approved by the Institutional Review Board of McLean Hospital.

Materials and methods

Sleep questionnaire

Each participant was scheduled for an intake session between 9:00 and 11:00 a.m. After provision of informed consent, each participant completed a number of self-report inventories about sleep and mood. For this analysis, we asked the participant to answer the question 'Do you ever have trouble falling asleep?' This item was identified as sleep initiation difficulty (SID). On the basis of the answer to this question, participants were categorized into SID or non-SID (NSID) groups. If the question was answered affirmatively, participants were also asked to indicate the weekly frequency of trouble falling asleep. Participants were also asked 'Do you ever have trouble staying asleep?' This item was identified as sleep maintenance difficulty (SMD). On the basis of the answer to this question, participants were categorized into SMD or non-SMD (NSMD) groups. If answered affirmatively, participants were also asked to report the weekly frequency of trouble staying asleep. In addition, we also asked participants 'How much sleep did you get last night?' This variable, identified as recent sleep, was scored in hours.

Neuroimaging

A 6-min resting-state functional MRI scan was obtained with eyes open. The scan was taken between 1:00 and 3:00 p.m. Neuroimaging was conducted on a 3T Siemens Tim Trio scanner (Siemens, Erlangen, Germany), using a 12-channel head coil. Initially, a T1-weighted 3D MPRAGE sequence (repetition time/echo time/flip angle = 2.1 s/2.25 ms/12°) over 128 sagittal slices (256 × 256 matrix) was obtained (slice thickness = 1.33 mm; voxel size = 1 × 1.33 × 1 mm). The functional connectivity scan comprised 180 images (3.5 mm thickness, 0 skip; 22.4 cm field of view; 64 × 64 acquisition matrix) over 34 axial interleaved slices obtained using a T2*-weighted blood oxygen level-dependent echoplanar imaging sequence (repetition time/echo time/flip angle = 2.0 s/30 ms/90°).

Image processing and analysis

Standard processing steps were completed in SPM8 (i.e. motion correction, slice-timing correction, coregistration, spatial normalization, and spatial smoothing at 6 mm full width at half maximum), and reslicing dimensions were 2 × 2 × 2 mm. Following preprocessing, functional connectivity analyses were undertaken with the Functional Connectivity Toolbox version 13i (*http://www.nitrc.org/projects/conn*) [9]. Data were band-pass filtered (0.008, 0.10 Hz), and physiological noise was removed using the aCompCor strategy [10]. Principle components analysis was used to eliminate the effects of white matter and cerebrospinal fluid. Motion parameters were also regressed out of the signal. To conduct region-of-interest to region-of-interest (ROI-to-ROI) analysis, eight ROIs from the Automated Anatomical Labeling (AAL) Atlas [11] were imported into the Functional Connectivity Toolbox. These bilateral ROIs are defined in detail by Tzourio-Mazoyer *et al.* [11] and include the following sensory and motor regions: (a) the primary visual cortex [i.e. cuneus – defined as 'the upper part of the medial wall of the occipital lobe, limited rostrally by the parieto-occipital sulcus and ventrally by the calcarine fissure. The cortex surrounding the calcarine fissure and its branches constituted the region of the primary visual area' (p. 285)]; (b) the primary auditory cortex [i.e. Heschl's gyrus – defined within the superior temporal gyrus bound by 'the deep temporal sulcus caudally and the posterior part of the circular sulcus of the insula rostrally' (p. 285)]; (c) the olfactory cortex – defined as 'the olfactory tubercle, lying in the caudal side of the gyrus rectus within the two branches of the fourth frontal sulcus, and the Broca's olfactory cortex located under the corpus callosum genu' (p. 285); and (d) the supplementary motor area (SMA) – defined as including 'the functional definition of the supplementary motor area and presupplementary motor area. Its posterior limit was the paracentral sulcus, its inferior limit was the cingulate sulcus, and we chose to use the Talairach atlas anterior limit: 20 mm ahead of the VAC plane' (p. 282) [11]. For each ROI, the mean time course across all voxels in the labeled mask region was extracted and correlated with the mean time course from each of the other ROIs using standard procedures in the

Functional Connectivity Toolbox. These correlation values were transformed to a Fishers *z*-score for each subject to permit second-level general linear model analyses. The *z*-scores reflecting the strength of functional connectivity were compared between the SID and NSID groups and between the SMD and NSMD groups using a one-tailed between-group *t*-test, with the number of hours of sleep obtained the previous night included as a nuisance covariate to control for potential effects of sleepiness or sleep debt on the connectivity findings. First, to control for multiple comparisons, all ROI-to-ROI connectivity maps were interrogated simultaneously set-wise at a *P*-value less than 0.10, with the false discovery rate corrected for multiple comparisons across all comparisons and ROIs in the network analysis. Second, within this network, individual ROI-to-ROI analyses were conducted for each seed region at a *P*-value less than 0.05, with false discovery rate corrected for the number of regions within each analysis.

Results

Self-report measures

Sleep initiation difficulty findings

The majority of participants reported that they did not have SID ($n = 33$; 57%), whereas a sizable minority reported that they did ($n = 25$, 43%). Of those who endorsed SID problems, nine (36%) had trouble getting to sleep less than one time per week, 11 (44%) had difficulty one to two times per week, and five (20%) reported having trouble three or more times per week. On average, those reporting trouble falling asleep had such difficulty on 1.71 nights per week (SD = 1.77).

Sleep maintenance difficulty findings

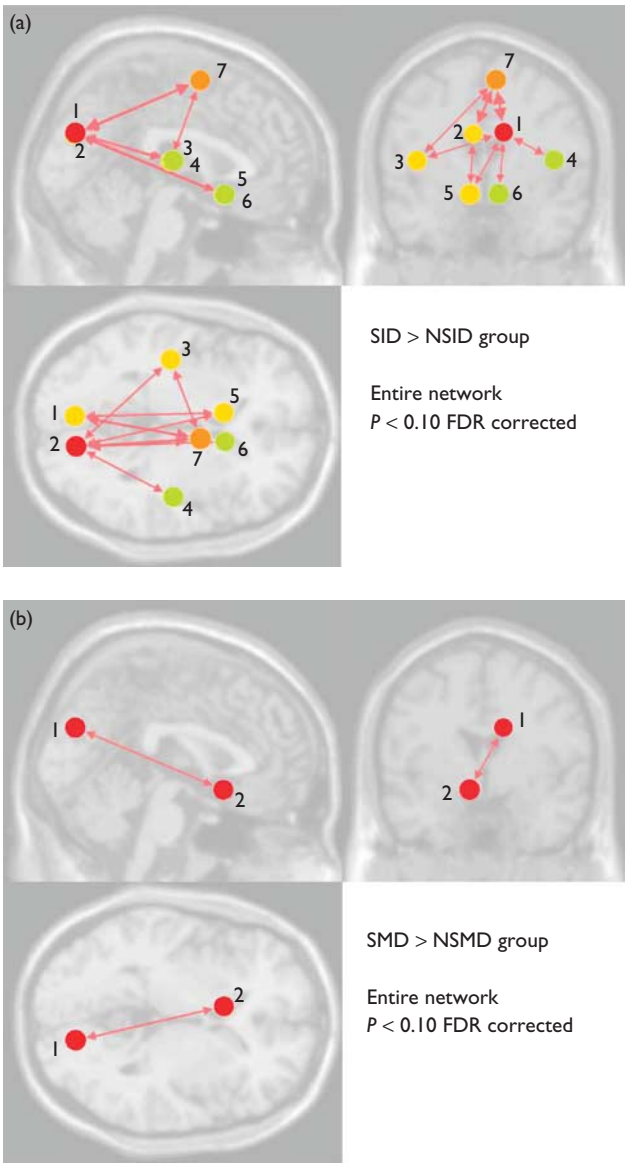
Most participants did not report problems with SMD ($n = 43$, 74%), whereas about a quarter did ($n = 14$, 24%). Among those endorsing sleep maintenance difficulties, three (21%) participants had problems less than once a week, seven (50%) had difficulty one to two times per week, and four (29%) had trouble three or more times per week. The mean number of nights per week an individual had trouble staying asleep was 1.82 (SD = 1.77) among those reporting SMD.

Neuroimaging

Sleep initiation difficulty findings

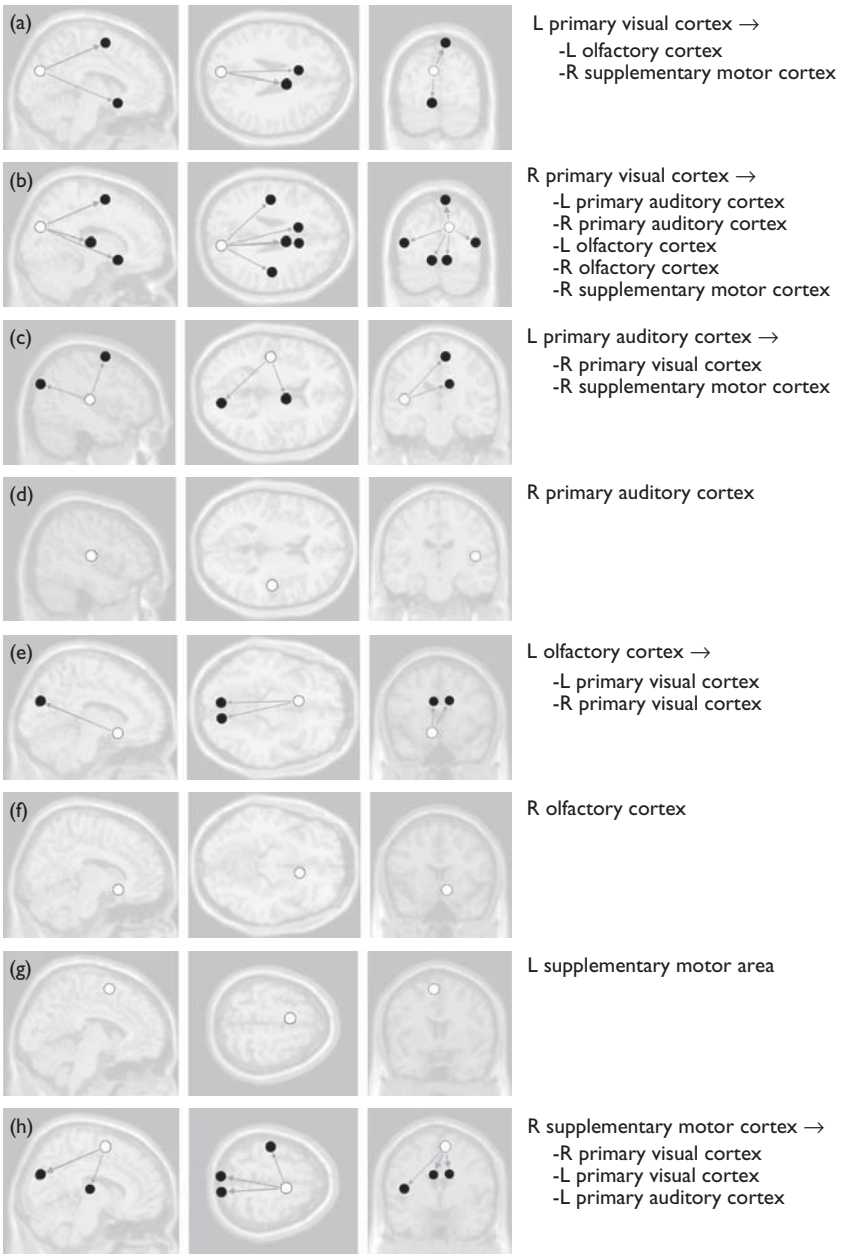
Compared with those without sleep onset complaints, participants reporting problems with falling asleep showed significantly greater functional connectivity across a network of sensory and motor activation regions (Fig. 1a). Notably, all eight ROIs remained significant when considered simultaneously as a set. Figure 2 shows the individual seed ROI-to-ROI connections for each seed region. Overall, difficulty in falling asleep was associated with increased functional connectivity between the primary visual cortex (i.e. cuneus) and other sensory regions such as the primary auditory cortex (Heschl's gyrus), olfactory cortex, and the supplementary motor cortex. The primary auditory cortex also showed greater connectivity with the supplementary motor cortex in the SID group compared with the NSID group. Statistics for these connections are listed in Table 1. There was no evidence of any connection showing greater

Fig. 1



Wire diagrams showing the network of regions with significantly greater functional connectivity between groups [$P < 0.10$, false discovery rate (FDR) corrected for all network comparisons and regions of interest (ROIs)]. (a) Compared with the no sleep initiation difficulty group (NSID), the sleep initiation difficulty (SID) group showed significantly greater functional connectivity among several regions including (1) the left visual cortex, (2) the right visual cortex, (3) the left auditory cortex, (4) the right auditory cortex, (5) the left olfactory cortex, (6) the right olfactory cortex, and (7) the right supplementary motor area. (b) Compared with the non-sleep maintenance difficulty (NSMD) group, the sleep maintenance difficulty (SMD) group showed greater functional connectivity between (1) the visual cortex and (2) the olfactory cortex.

Fig. 2



Individual connectivity maps for each seed ROI-to-ROI comparison that was significantly greater among the SID group compared with the NSID group ($P < 0.05$, false discovery rate corrected). (a) The left primary visual cortex was functionally connected to the left olfactory cortex and right supplementary motor area; (b) the right primary visual cortex was functionally connected to the left and right primary auditory cortex, left and right olfactory cortex, and the right supplementary motor area; (c) the left primary auditory cortex was functionally connected to the right primary visual cortex and right supplementary motor area; (d) the right primary auditory cortex was not functionally connected to other ROIs; (e) the left olfactory cortex was functionally connected to the left and right primary visual cortex; (f) the right olfactory cortex was not functionally connected to other ROIs; (g) the left supplementary motor area was not functionally connected to other ROIs; (h) the right supplementary motor area was functionally connected to the right and left visual cortex and the left primary auditory cortex. NSID, non-sleep initiation difficulty; ROI, region of interest; SID, sleep initiation difficulty.

anticorrelated patterns among the SID group compared with the NSID group.

Sleep maintenance difficulty findings

Individuals reporting problems with maintaining sleep showed greater connectivity between the primary visual cortex and the olfactory cortex compared with the NSMD group, even after setwise correction for all comparisons (Fig. 1b). Figure 3 presents the results from the individual seed ROI-to-ROI analyses, again showing that participants in the SMD group showed greater functional connectivity between the visual cortex and the olfactory

Table 1 ROI-to-ROI functional connectivity statistics for an individual seed region *t*-test comparison between the SID and non-SID groups

Target region	β	*t*	*d.f.*	P_{unc}	P_{FDR}
Primary visual cortex (L)					
Supplementary motor area (R)	0.20	3.67	55	0.0003	0.0019*
Olfactory cortex (L)	0.11	2.34	55	0.0114	0.0399*
Primary visual cortex (R)					
Supplementary motor area (R)	0.22	3.86	55	0.0002	0.0011*
Primary auditory cortex (L)	0.13	2.48	55	0.0081	0.0210*
Primary auditory cortex (R)	0.13	2.44	55	0.0090	0.0210*
Olfactory cortex (L)	0.10	2.26	55	0.0139	0.0243*
Olfactory cortex (R)	0.11	2.02	55	0.0242	0.0338*
Primary auditory cortex (L)					
Supplementary motor area (R)	0.14	2.51	55	0.0076	0.0282*
Primary visual cortex (R)	0.13	2.48	55	0.0081	0.0282*
Primary auditory cortex (R)	–	–	–	–	–
Olfactory cortex (L)					
Primary visual cortex (L)	0.11	2.34	55	0.0114	0.0486*
Primary visual cortex (R)	0.10	2.26	55	0.0139	0.0486*
Olfactory cortex (R)					
Primary visual cortex (R)	0.11	2.02	55	0.0242	0.1692*
Supplementary motor area (L)	–	–	–	–	–
Supplementary motor area (R)					
Primary visual cortex (R)	0.22	3.86	55	0.0002	0.0001*
Primary visual cortex (L)	0.20	3.67	55	0.0003	0.0001*
Primary auditory cortex (L)	0.14	2.51	55	0.0076	0.0177*

FDR, false discovery rate; NSID, non-sleep initiation difficulty; P_{FDR}, *P*-false discovery corrected for number of regions analyzed; P_{unc}, *P*-uncorrected; ROI, region of interest; SID, sleep initiation difficulty.
*$P<0.10$ FDR setwise corrected for all comparisons across the entire network.

cortex compared with the NSMD group. Table 2 presents the statistics associated with this connectivity. No anticorrelated connectivity differences were observed.

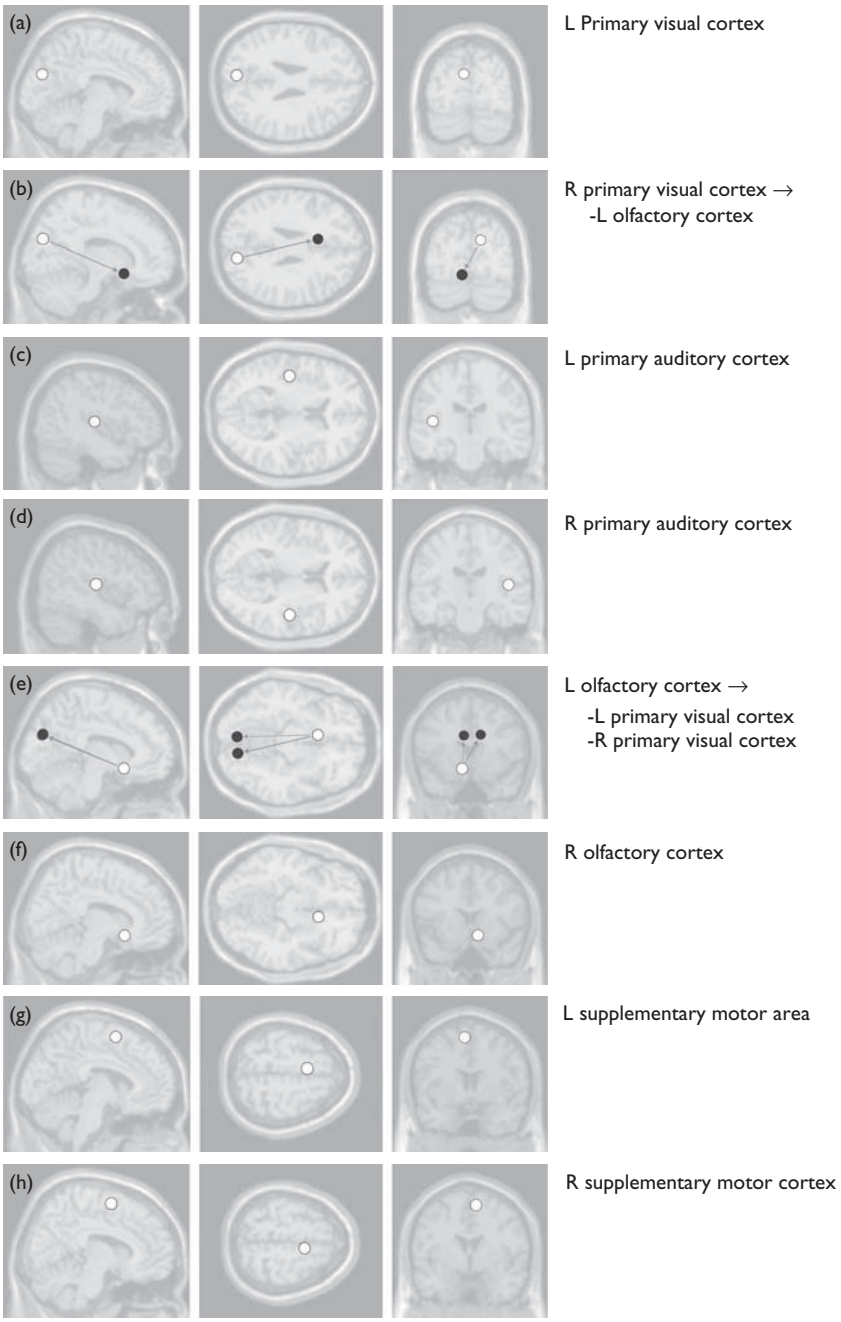
Discussion

We examined resting-state functional connectivity differences between healthy individuals endorsing or denying two types of insomnia-related sleep problems, focusing on the connectivity patterns between several primary sensory processing and motor action preparatory areas. Overall, we found rates of sleep problems similar to those reported previously in the general population [4]. Moreover, participants who reported difficulty in falling asleep showed significantly greater resting-state functional connectivity between several hypothesized regions than those without such problems. Specifically, we found increased connectivity between the primary visual cortex and the supplementary motor areas, as well as between the primary visual and auditory regions and between the auditory cortex and the supplementary motor regions, in those reporting difficulty in falling asleep. The olfactory cortex also showed modestly greater connectivity with the primary visual cortex in the SID group compared with the NSID group. We also examined the functional connectivity within the same network among those reporting difficulty in maintaining sleep. Those reporting SMD showed greater functional connectivity between the primary visual cortex and the olfactory cortex while resting with their eyes open. These patterns of increased functional connectivity were observed even after controlling for the amount of sleep obtained the night preceding the scan, suggesting that the findings are not state related but instead appear to reflect a stable pattern of functioning that may contribute to the reported sleep difficulties.

Our findings are consistent with the hyperarousal model of insomnia [1,5], which suggests that PI is associated with heightened arousal of the central nervous system. This excess arousal is proposed to be manifested as exaggerated cortical, somatic, and cognitive activation, which leads to increased sensory and information processing, ultimately hampering the ability to initiate or maintain sleep [1,6]. We found that individuals reporting difficulty in falling asleep showed significantly greater functional connectivity among several primary sensory regions, as would be expected in the case of increased sensory processing. We also found that those with problems in falling asleep showed greater functional connectivity between these sensory regions and the premotor cortex, a region implicated in the intention to move, the activation of motor plans, and the spontaneous generation of movement [12]. In practical terms, one implication of this finding is that stimulation of one sensory modality, whether internally or externally generated, might be associated with increased activation of other sensory and motor preparatory regions, for example, as in the case in which the sound of the ticking clock leads to activation of the primary visual cortex, increased visual awareness of the environment, and spontaneous body movement. Greater connectivity among these sensory and motor activating regions could conceivably sustain arousal and enhance unwanted sensory awareness, leading to difficulty in falling asleep or awakening easily from sleep.

It is interesting that SID was associated with extensive functional connectivity among the primary sensory and supplementary motor cortex, whereas SMD only showed evidence of greater functional connectivity between the primary visual cortex and the olfactory cortex. This suggests that state functional connectivity observed during waking rest may be more strongly associated with processes interfering with sleep onset than with processes occurring during the sleep state that lead to premature waking. In line with this, some evidence from research examining event-related potentials during sleep suggests that individuals with insomnia show reduced sensory gating of auditory stimuli and a failure to produce stimulus-related K-complexes compared with good sleepers [13]. The K-complex, an EEG waveform commonly seen during stage 2 NREM sleep, is believed to play a role in protecting sleep against spontaneous waking [14]. Thus, problems with SMD may be more related to these aspects of sensory gating and EEG abnormalities than to increased functional connectivity among various sensory and supplementary motor regions. However, the finding of increased connectivity between the medial olfactory cortex and the visual cortex in those who report difficulty

Fig. 3



Individual connectivity maps for each seed ROI-to-ROI comparison that was significantly greater among the SMD group compared with the NSMD group ($P < 0.05$, false discovery rate corrected). (a) The left primary visual cortex was not functionally connected with other ROIs; (b) the right primary visual cortex was functionally connected with the left olfactory cortex; (c) the left primary auditory cortex was not functionally connected with other ROIs; (d) the right primary auditory cortex was not functionally connected with other ROIs; (e) the left olfactory cortex was functionally connected with the left and right primary visual cortex; (f) the right olfactory cortex was not functionally connected with other ROIs; (g) the left supplementary motor area was not functionally connected with other ROIs; (h) the right supplementary motor area was not functionally connected with other ROIs.

in maintaining sleep is intriguing, suggesting a potential sleep disrupting or alerting network that involves these two systems in this group of individuals. Recent data suggest that the olfactory tubercle, one structure located within the olfactory cortex ROI, is involved in cross-modal sensory convergence of smell and sound [15], and it is conceivable that this region may be involved in other aspects of cross-modal convergence. Early work has suggested that individuals with an intolerance to chemical odors show objectively poorer sleep patterns than those

Table 2 ROI-to-ROI functional connectivity statistics for an individual seed region *t*-test comparison between SMD and non-SMD groups

Target Region	β	*T*	*d.f.*	P_{unc}	P_{FDR}
Primary visual cortex (L)	–	–	–	–	–
Primary visual cortex (R)	–	–	–	–	–
Olfactory cortex (L)	0.15	2.81	55	0.0034	0.0240*
Primary auditory cortex (L)	–	–	–	–	–
Primary auditory cortex (R)	–	–	–	–	–
Olfactory cortex (L)					
Primary visual cortex (R)	0.15	2.81	55	0.0034	0.0240*
Primary visual cortex (L)	0.13	2.29	55	0.0130	0.0454
Olfactory cortex (R)	–	–	–	–	–
Supplementary motor area (L)	–	–	–	–	–
Supplementary motor area (R)	–	–	–	–	–

FDR, false discovery rate; NSMD, non-sleep maintenance difficulty; P_{FDR}, *P*-false discovery corrected for number of regions analyzed; P_{unc}, *P*-uncorrected; ROI, region of interest; SMD, sleep maintenance difficulty.
*$P<0.10$ FDR setwise corrected for all comparisons across the entire network.

without such sensitivity [16], and more recent evidence indicates that individuals with better odor identification abilities are more resistant to sleep deprivation [17]. Although some data suggest that odors can influence the emotional tone of dreams [18] or can enhance the alerting effect of trigeminal nerve stimulation [19], most studies have failed to find an alerting effect of specific odors when presented in isolation during sleep [20]. No study has compared the sensitivity of good and poor sleepers to odors yet.

Thus far, surprisingly few studies have used functional neuroimaging to study insomnia-related problems [21]. An early study found hypoperfusion within cortical regions and basal ganglia in a small sample of five patients with PI [22]. Similarly, Altena *et al.* [23] found that insomnia is associated with reduced functional activation within the medial prefrontal cortex during verbal fluency tasks, which recovered following cognitive behavioral treatment. To our knowledge, only one other study has examined the resting-state functional connectivity of individuals with insomnia-related problems and found that patients with PI show reduced functional connectivity between the amygdala and regions such as the insula, thalamus, and striatum [24]. However, the same study also found increased connectivity of the amygdala with the premotor and sensory–motor cortex. This is consistent with the present findings of increased functional connectivity between the primary sensory and the supplementary motor cortex.

One of the strengths of the present study is the relatively large sample size; however, our findings are limited by the use of a self-report measure to identify sleep difficulties. Consequently, no clinical diagnosis of sleep disorders or PI was made. In fact, our sample was screened to exclude individuals with medical or psychiatric disorders that may affect sleep, but no specific screening for clinical sleep disorders was conducted. This likely restricted the range of sleep disturbances observed. Future research should examine connectivity of these same regions in clinical patients with PI. Finally, because the data are cross-sectional and involve correlational techniques, the causal direction of these results cannot be inferred.

Conclusion

Consistent with the predictions of the hyperarousal model of insomnia, healthy individuals reporting difficulty in falling asleep showed significantly greater functional connectivity among several primary sensory regions and the supplementary motor area compared with those without such complaints. Increased functional connectivity among these regions may contribute to sustained sensory processing of environmental stimuli, which may prolong the latency to sleep.

Acknowledgements

This study was supported by a USAMRAA grant (W81XWH-09-1-0730).

Conflicts of interest

There are no conflicts of interest.

References

1 Riemann D, Spiegelhalder K, Feige B, Voderholzer U, Berger M, Perlis M, *et al.* The hyperarousal model of insomnia: a review of the concept and its evidence. *Sleep Med Rev* 2010; **14**:19–31.
2 American-Psychiatric-Association. *Diagnostic and Statistical Manual of Mental Disorders*. Washington, DC: American Psychiatric Association; 1994.
3 Ohayon MM. Epidemiology of insomnia: what we know and what we still need to learn. *Sleep Med Rev* 2002; **6**:97–111.
4 Ohayon MM, Reynolds CF III. Epidemiological and clinical relevance of insomnia diagnosis algorithms according to the DSM-IV and the International Classification of Sleep Disorders (ICSD). *Sleep Med* 2009; **10**:952–960.
5 Perlis ML, Giles DE, Mendelson WB, Bootzin RR, Wyatt JK. Psychophysiological insomnia: the behavioural model and a neurocognitive perspective. *J Sleep Res* 1997; **6**:179–188.
6 Perlis ML, Merica H, Smith MT, Giles DE. Beta EEG activity and insomnia. *Sleep Med Rev* 2001; **5**:363–374.
7 Spiegelhalder K, Regen W, Feige B, Holz J, Piosczyk H, Baglioni C, *et al.* Increased EEG sigma and beta power during NREM sleep in primary insomnia. *Biol Psychol* 2012; **91**:329–333.
8 Wolynczyk-Gmaj D, Szelenberger W. Waking EEG in primary insomnia. *Acta Neurobiol Exp (Warsz)* 2011; **71**:387–392.
9 Whitfield-Gabrieli S, Nieto-Castanon A. Conn: a functional connectivity toolbox for correlated and anticorrelated brain networks. *Brain Connect* 2012; **2**:125–141.
10 Behzadi Y, Restom K, Liau J, Liu TT. A component based noise correction method (CompCor) for BOLD and perfusion based fMRI. *Neuroimage* 2007; **37**:90–101.
11 Tzourio-Mazoyer N, Landeau B, Papathanassiou D, Crivello F, Etard O, Delcroix N, *et al.* Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. *Neuroimage* 2002; **15**:273–289.
12 Nachev P, Kennard C, Husain M. Functional role of the supplementary and pre-supplementary motor areas. *Nat Rev Neurosci* 2008; **9**:856–869.
13 Hairston IS, Talbot LS, Eidelman P, Gruber J, Harvey AG. Sensory gating in primary insomnia. *Eur J Neurosci* 2010; **31**:2112–2121.
14 Forget D, Morin CM, Bastien CH. The role of the spontaneous and evoked K-complex in good-sleeper controls and in individuals with insomnia. *Sleep* 2011; **34**:1251–1260.
15 Wesson DW, Wilson DA. Smelling sounds: olfactory–auditory sensory convergence in the olfactory tubercle. *J Neurosci* 2010; **30**:3013–3021.
16 Bell IR, Bootzin RR, Ritenbaugh C, Wyatt JK, DeGiovanni G, Kulinovich T, *et al.* A polysomnographic study of sleep disturbance in community elderly with self-reported environmental chemical odor intolerance. *Biol Psychiatry* 1996; **40**:123–133.

17 Killgore WDS, McBride SA, Killgore DB, Balkin TJ, Kamimori GH. Baseline odor identification ability predicts degradation of psychomotor vigilance during 77 h of sleep deprivation. *Int J Neurosci* 2008; **118**: 1207–1225.
18 Schredl M, Atanasova D, Hormann K, Maurer JT, Hummel T, Stuck BA. Information processing during sleep: the effect of olfactory stimuli on dream content and dream emotions. *J Sleep Res* 2009; **18**:285–290.
19 Stuck BA, Baja J, Lenz F, Herr RM, Heiser C. Co-stimulation with an olfactory stimulus increases arousal responses to trigeminal stimulation. *Neuroscience* 2011; **176**:442–446.
20 Carskadon MA, Herz RS. Minimal olfactory perception during sleep: why odor alarms will not work for humans. *Sleep* 2004; **27**:402–405.
21 Drummond SP, Smith MT, Orff HJ, Chengazi V, Perlis ML. Functional imaging of the sleeping brain: review of findings and implications for the study of insomnia. *Sleep Med Rev* 2004; **8**:227–242.
22 Smith MT, Perlis ML, Chengazi VU, Pennington J, Soeffing J, Ryan JM, *et al*. Neuroimaging of NREM sleep in primary insomnia: a Tc-99-HMPAO single photon emission computed tomography study. *Sleep* 2002; **25**:325–335.
23 Altena E, Van Der Werf YD, Sanz-Arigita EJ, Voorn TA, Rombouts SA, Kuijer JP, *et al*. Prefrontal hypoactivation and recovery in insomnia. *Sleep* 2008; **31**:1271–1276.
24 Huang Z, Liang P, Jia X, Zhan S, Li N, Ding Y, *et al*. Abnormal amygdala connectivity in patients with primary insomnia: evidence from resting state fMRI. *Eur J Radiol* 2012; **81**:1288–1295.

J Sleep Res. (2013) Regular Research Paper

Habitual 'sleep credit' is associated with greater grey matter volume of the medial prefrontal cortex, higher emotional intelligence and better mental health

MAREEN WEBER, CHRISTIAN A. WEBB, SOPHIE R. DELDONNO, MAIA KIPMAN, ZACHARY J. SCHWAB, MELISSA R. WEINER and WILLIAM D. S. KILLGORE

Social, Cognitive and Affective Neuroscience Laboratory, McLean Hospital, Harvard Medical School, Belmont, MA, USA

Keywords
emotional intelligence, excess sleep, medial prefrontal cortex, psychopathology, voxel-based morphometry

Correspondence
William D. S. Killgore, PhD, Social, Cognitive and Affective Neuroscience Laboratory, McLean Hospital, Harvard Medical School, 115 Mill Street, Belmont, MA 02478, USA.
Tel.: 617-855-3166;
fax: 617-855-2770;
e-mail: killgore@mclean.harvard.edu

Accepted in revised form 9 March 2013;
received 14 November 2012

DOI: 10.1111/jsr.12056

SUMMARY

In modern society, people often fail to obtain the amount of sleep that experts recommend for good health and performance. Insufficient sleep can lead to degraded cognitive performance and alterations in emotional functioning. However, most people also acknowledge that on a regular basis they obtain more sleep than they subjectively perceive they need at a minimum to stave off performance decrements, a construct we describe as subjective 'sleep credit'. Few people would contest the notion that getting more sleep is better, but data on both behavioural and neuroanatomical correlates of 'sleep credit' are surprisingly limited. We conducted a voxel-based morphometric study to assess cerebral grey matter correlates of habitually sleeping more than one's subjective requirements. We further tested whether these structural correlates are associated with perceived emotional intelligence and indices of psychopathology while controlling for age, gender, and total intracranial volume. In a sample of 55 healthy adults aged 18–45 years (28 males, 27 females), whole-brain multiple regression showed that habitual subjective 'sleep credit' was correlated positively with grey matter volume within regions of the left medial prefrontal cortex and right orbitofrontal gyrus. Volumes were extracted and regressed against self-report emotion and psychopathology indices. Only grey matter volume of the medial prefrontal cortex cluster correlated with greater emotional intelligence and lower scores on several indices of psychopathology. Findings converge with previous evidence of the role of the medial prefrontal cortex in the relationship between sleep and emotional functioning, and suggest that behaviour and brain structure vary with habitual 'sleep credit'.

INTRODUCTION

In today's society, many healthy adults often sleep less than the 7–8 h per night recommended by most experts (Ferrara, 2001; National Sleep Foundation, 2005). Both acutely and habitually insufficient sleep have been demonstrated to affect various aspects of daytime functioning adversely, such as sleep propensity, attention and alertness (Banks and Dinges, 2007; Punjabi *et al.*, 2003; Van Dongen and Maislin, 2003). Relative to being well rested, prolonged sleep debt may also increase somatic complaints and symptoms of depression, anxiety and paranoia (Kahn-Greene *et al.*, 2007). Even measures of self-perceived emotional intelligence may also be impacted negatively by sleep deprivation. More specifically, previous research indicates decreases in both global emotional intelligence, as well as in inter- and intrapersonal functioning (e.g. lower empathy towards others; reduced self-regard) and stress management (e.g. impaired impulse control) following prolonged sleep deprivation compared to rested baseline (Killgore *et al.*, 2008). Thus, there is clear and ample evidence that people do not sleep as much as is recommended physiologically, and that insufficient sleep

impairs daytime functioning. Interestingly, however, some data also suggest that approximately 40% of adults get more sleep than they think they need subjectively (National Sleep Foundation, 2005). One could argue that getting more sleep than needed subjectively would benefit behaviour and possibly even counteract the effects of physiologically insufficient sleep. Indeed, Rupp and colleagues showed in a series of studies that a brief period of 'banking sleep' by sleeping for longer than normal before a period of insufficient sleep enhances resilience to and recovery from the actual sleep loss (Rupp *et al.*, 2009a,b). One relatively unexplored aspect of the relationship between sleep and behaviour concerns whether sleeping more than needed on a habitual basis (i.e. 'sleep credit') is also associated with behavioural or emotional benefits, and whether this may be reflected in specific differences in regional brain volume.

For chronic sleep restriction, at least in the context of sleep disorders (e.g. chronic insomnia, obstructive sleep apnea, narcolepsy) and daytime sleepiness in otherwise healthy adults, persistently insufficient sleep and excessive daytime sleepiness have been linked to reduced grey matter volume, particularly of the ventromedial and orbitofrontal cortex (Altena *et al.*, 2010; Joo *et al.*, 2010; Killgore *et al.*, 2012b; Morrell, 2003). The mechanisms underlying this relationship remain unknown. Reduced grey matter could emerge as a function of insufficient sleep. However, animal research has not demonstrated conclusively an adverse effect of chronic sleep restriction on neuronal health (Cirelli *et al.*, 1999), although there is some recent evidence that sleep deprivation can reduce axonal sprouting in animal models of stroke (Gao *et al.*, 2010; Zunzunegui *et al.*, 2011) and may inhibit hippocampal volume and neurogenesis in laboratory animals (Mueller *et al.*, 2011; Novati *et al.*, 2011). In humans, no grey matter volume changes were observed in patients with obstructive sleep apnea following successful intervention (O'Donoghue, 2005). Thus, it may be that reduced grey matter in this region may serve as a diathesis that precedes and increases vulnerability to disordered sleep, but it is also conceivable that increased grey matter in this region may emerge as a consequence of sleeping more than the minimum needed to function without impairment. However, given the lack of empirical data on sleep and brain structure, the first step would be to demonstrate this association in humans. Therefore, the present study aimed to investigate voxel-based morphological correlates of sleeping in excess of minimal subjective requirements in a sample of healthy adults. In addition, we also attempted to test whether morphological correlates of 'sleep credit' would be associated with indices of psychopathology and emotional intelligence that have been shown previously to be sensitive to sleep loss. Based on the literature reviewed above, we hypothesized that sleeping habitually in excess of minimal subjective requirements would be associated with increased grey matter volume in ventromedial and orbitofrontal cortices. In addition, we hypothesized that grey matter volume in this brain region would be correlated negatively with lower scores on indices of psychopathology and positively with greater emotional intelligence.

METHODS

Participants

Using posted flyers and internet advertisements, we recruited 55 healthy right-handed adults (mean age 30.74 $\pm$ 8.13, range 18–45; 28 males, 27 females; mean years of education 14.96 $\pm$ 2.17, range 11–20) from the Boston metropolitan area. There was no age difference between females and males. All participants were native English speakers and underwent a detailed screening interview to determine eligibility. Based on this screening, all participants included in the study were deemed healthy (i.e. no history of neurological, psychiatric, alcohol, illicit substance use disorders or sleep disorders). Any other conditions that may influence magnetic resonance imaging (MRI; e.g. chronic pain that would not allow the subject to remain still in the scanner) and psychoactive medications (e.g. antidepressants, analgesics, anticonvulsants) were also exclusionary. Participants were compensated at a rate of $25 per hour. The McLean Hospital Institutional Review Board approved this research, which was conducted in accordance with the 1964 Declaration of Helsinki. Prior to study participation, each participant provided written informed consent.

Materials and procedures

On the day of the MRI scan, participants responded to two open-ended questions on sleep habits: (i) how much do you typically sleep on weeknights (Sunday to Thursday); and (ii) how much do you typically sleep on weekend nights (Friday to Saturday)? In addition, all participants completed the following statement on subjective sleep need: 'If I get less than __ hours of sleep, I notice an impairment in my ability to function at work'. Participant response to the first two items was used to calculate the weighted average habitual sleep (in hours). 'Sleep credit' was conceptualized as the difference between the weighted average habitual sleep and the subjectively reported minimum hours of sleep necessary until functional impairment is noticed.

In addition, participants completed the Bar-On Emotional Quotient Inventory (EQ-i; Bar-On, 2006), a self-report measure of trait emotional intelligence. The inventory contains 125 items yielding a total emotional quotient plus five composite scores (interpersonal, intrapersonal, adaptability, stress management, general mood). Individual items are answered on a five-point Likert scale ranging from 'very seldom or not true of me' to 'very often true of me or true of me'. The interpersonal composite score reflects perceived empathy and interpersonal skills, whereas the intrapersonal composite provides a measure of self-perceived awareness of personal emotions and self-regard. Adaptability reflects the perceived ability to

scrutinize challenging circumstances objectively, to resolve them and to adapt flexibly to changing situations. Stress management provides a measure of tolerance of, and perceived self-control during, taxing or challenging situations. Finally, the general mood composite reflects self-reported positive thinking and overall satisfaction with personal life. Based on previous research showing that sleep loss affects specific scales of the EQ-i (Killgore *et al.*, 2008), we restricted our analyses to the total emotional quotient and the interpersonal, intrapersonal and stress management composites.

Every participant also completed the computerized Personality Assessment Inventory (PAI; Morey, 1991) as an index of several dimensions of psychopathology. The PAI contains 344 statements that are rated using one of four response options ('false, not at all true', 'slightly true', 'mainly true', 'very true'). It yields 11 clinical subscales (somatic complaints, anxiety, anxiety-related disorders, depression, mania, paranoia, schizophrenia, borderline features, antisocial features, drug-related problems, alcohol-related problems). Based on previous findings from the literature showing that sleep deprivation affects specific scales on the PAI (Kahn-Greene *et al.*, 2007), we restricted our primary analyses to four clinical scales (i.e. somatic complaints, anxiety, depression, paranoia). Raw scores for each scale and subscale used in this study were converted into T scores based on the normative data provided with the scoring programme and in the test manual (Morey, 1991).

MRI parameters

We acquired structural magnetic resonance images at 3.0 Tesla using a 12-channel head coil (Siemens Tim Trio, Erlangen, Germany) and a T1-weighted three-dimensional MPRAGE sequence (TR/TE/flip angle: 2.1s/2.25 ms^{-1}/12°; 128 sagittal slices; 256 × 256 matrix; in-plane resolution: 1 × 1 × 1 mm; slice thickness: 1.33 mm).

Voxel-based morphometry

The VBM8 toolbox in SPM8 was used for preprocessing of structural images (Wellcome Department of Imaging Neuroscience Group, London, UK; http://www.fil.ion.ucl.ac.uk/spm/; http://dbm.neuro.uni-jena.de/vbm.html). The modulated voxel-based morphometry (i.e. grey matter volume was corrected for total brain volume) applied default settings. That is, each structural image was first DARTEL-normalized to match the Montreal Neurological Institute template. Then, a fully automated algorithm within SPM8 segmented each image into grey matter, white matter and cerebrospinal fluid. Finally, normalized grey matter images were smoothed with an 8-mm full-width at half-maximum isotropic Gaussian kernel.

Statistical analysis

The statistical analysis involved three nested steps. The first step tested the association between the amount of 'sleep credit' and voxelwise grey matter volume. Thus, normalized smoothed grey matter images were entered into a whole-brain general linear model in SPM8 using a threshold of $P < 0.001$, uncorrected, with a cluster extent $k \geq 90$, which was determined statistically as the expected number of voxels per cluster that would be expected by chance based on the theory of Gaussian random fields applied to this analysis (as provided in the standard VBM8 output). Age and gender were included as nuisance covariates. The second step tested whether the grey matter volume clusters from the first step were associated with scores on the emotional intelligence and psychopathology indices. Here, eigenvariates, as extracted from each significant cluster, were entered stepwise as regressors into a series of multiple regression models in IBM SPSS Statistics for Macintosh version 20 (IBM Corp., Armonk, NY, USA). To limit type I error, we ran one primary analysis for the total score of the EQ-i and PAI, respectively (i.e. five models: EQ-i total; PAI somatization; PAI anxiety; PAI depression; PAI paranoia) using a Bonferroni-corrected significance threshold $P < 0.01$ for each model. The third analysis step examined associations between grey matter volume and composite scores of the two tests used (i.e. EQ-i: interpersonal, intrapersonal, stress management; PAI: somatization conversion/somatization/health concerns; anxiety cognitive/affective/physiological; depression cognitive/affective/physiological; paranoia hypervigilance/persecution/resentment). Follow-up analyses were conducted only for significant primary analyses and significant regressors. Normal distribution of all dependent variables was tested with the Shapiro–Wilk test in SPSS. For normally distributed data (i.e. all EQ-i composites), we derived Pearson correlations, whereas Spearman correlations were computed for the non-normally distributed composite scores (i.e. all PAI composites). Again, per inventory, we applied a Bonferroni-corrected significance threshold $P < 0.017$ ($\alpha = 0.05$ divided by three subscores).

RESULTS

On average, self-reported habitual sleep was 7.46 h [standard deviation (SD) = 0.80, range 5.5–9.0]. The minimum hours of sleep needed subjectively before functional impairment was noticeable to the individual varied greatly from 2 to 10 h (mean = 5.65, SD = 1.35). Therefore, on average, participants 'banked' 1.8 h of 'sleep credit' on a habitual basis (SD = 1.49, range −3 to 5.5). The mean total EQ-i was 100.60 (SD = 13.89, range 69–126; interpersonal: mean = 99.98, SD = 14.76, range 59–125; intrapersonal: mean = 100.55, SD = 14.88, range 59–125; stress management: mean = 102.89, SD = 12.21, range 76–125). All mean PAI scale and subscale scores were within normal ranges (somatic complaints: mean = 46.07, SD = 6.88, range 39–89; anxiety: mean = 47.47, SD = 9.39, range 35–73; depression: mean = 47.20, SD = 10.82, range 36–101; paranoia: mean = 51.53, SD = 10.46, range 32–74).

As evident in Fig. 1, greater 'sleep credit' correlated with greater grey matter volume in two clusters: (i) left gyrus

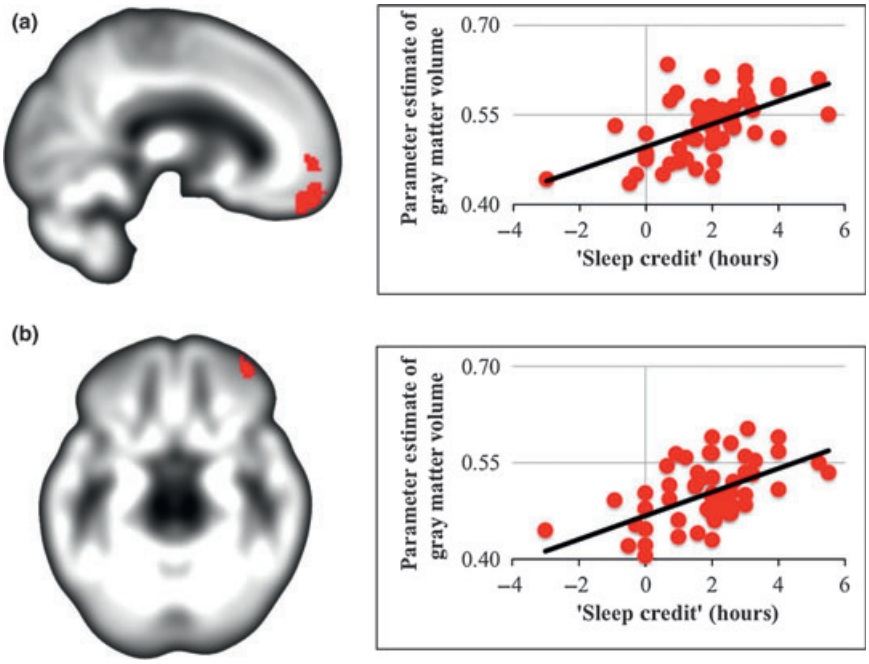


Figure 1. (a) Sagittal view of the left gyrus rectus/orbitofrontal gyrus cluster (overlaid on sample-specific T1 mean image) that was correlated positively with sleeping in excess of subjective need and the corresponding scatterplot showing the relationship between sleeping more than needed subjectively (in hours) and average grey matter volume for the cluster located at Montreal Neurological Institute (MNI) coordinates $x = -6$, $y = 52$, $z = -21$. (b) Axial view of the right middle orbitofrontal gyrus cluster (overlaid on sample-specific T1 mean image) that was correlated positively with sleeping in excess of subjective need and the corresponding scatterplot showing the relationship between 'sleep credit' (i.e. sleeping more than needed subjectively) and average grey matter volume for the cluster located at MNI coordinates $x = 39$, $y = 51$, $z = -18$.

rectus/superior and medial orbital frontal gyrus (OFG; 892 voxels, $T = 4.81$, peak-level Montreal Neurological Institute (MNI) coordinates: $x = -6$, $y = 52$, $z = -21$) and (ii) right middle OFG (149 voxels, $T = 4.43$, peak-level MNI coordinates: $x = 39$, $y = 51$, $z = -18$).

Table 1 presents results of the multiple regression analysis on the total EQ-i. Only grey matter volume of the cluster comprising the left gyrus rectus, superior and medial OFG correlated with total EQ-i. This means that greater grey matter in this medial PFC cluster was associated with greater global perceived emotional intelligence. Follow-up Pearson correlations with Bonferroni correction to $P < 0.017$ showed positive associations between this cluster's grey matter volume and the interpersonal subscale only [interpersonal: $r = 0.38$, $P < 0.017$; intrapersonal: $r = 0.28$, not significant (NS); stress management: $r = 0.23$, NS].

Table 2 presents results of the multiple regression analyses on the PAI clinical scales somatization, depression, anxiety and paranoia. Similar to the findings for the EQ-i, only grey matter volume of left gyrus rectus/medial and superior OFG correlated with PAI psychopathology. Overall, greater grey matter volume in this cluster in the medial PFC correlated with lower scores on indices of psychopathology, but this was true only for somatic complaints, depression and paranoia, but not anxiety. For PAI somatization, none of the follow-up Spearman correlations survived Bonferroni correction (conversion: $r = -0.29$, $P = 0.03$; somatization: $r = -0.15$, $P = 0.29$; health concerns: $r = -0.29$, $P = 0.03$). For PAI depression, follow-up Spearman correlations showed negative associations between grey matter volume of this cluster in the medial PFC and cognitive and physiological, but not affective, symptoms of depression (cognitive: $r = -0.34$, $P < 0.017$; affective: $r = -0.29$, $P = 0.03$; physiological: $r = -0.36$, $P < 0.017$). For PAI paranoia, follow-up Spearman correlations also showed negative associations between grey matter volume of this

Table 1 Stepwise linear regression of grey matter volume on emotional intelligence

Total EQ-i	*B*	*SE B*	ΔR^2	β
Step 1				
Constant	47.84	18.81		
L. gyrus rectus/superior and medial OFG	99.31	35.26	0.13	0.36*
Step 2				
Constant	44.95	20.77		
L. gyrus rectus/superior and medial OFG	92.30	41.00	0.13	0.34
R. middle OFG	13.22	38.55	0.01	0.05

EQ-i, emotional quotient; OFG, orbitofrontal gyrus; SE, standard error.
*$P < 0.01$.

Table 2 Stepwise linear regression of grey matter volume on hypothesized PAI psychopathology scales

	B	*SE B*	ΔR^2	β
PAI somatization				
Step 1				
Constant	47.84	18.81		
L. gyrus rectus/superior and medial OFG	99.31	35.26	0.13	0.36*
Step 2				
Constant	44.95	20.77		
L. gyrus rectus/superior and medial OFG	92.30	41.00	0.13	0.34
R. middle OFG	13.22	38.55	0.01	0.05
PAI anxiety				
Step 1				
Constant	76.16	13.05		
L. gyrus rectus/superior and medial OFG	−53.99	24.46	0.08	−0.29
Step 2				
Constant	72.64	14.38		
L. gyrus rectus/superior and medial OFG	−62.49	28.38	0.08	−0.34
R. middle OFG	16.03	26.68	0.01	0.09
PAI depression				
Step 1				
Constant	96.64	14.15		
L. gyrus rectus/superior and medial OFG	−93.07	26.53	0.19	−0.43*
Step 2				
Constant	103.90	15.45		
L. gyrus rectus/superior and medial OFG	−75.52	30.50	0.19	−0.35
R. middle OFG	−33.13	28.67	0.02	−0.16
PAI paranoia				
Step 1				
Constant	106.14	13.20		
L. gyrus rectus/superior and medial OFG	−102.80	24.74	0.25	−0.40*
Step 2				
Constant	114.63	14.30		
L. gyrus rectus/superior and medial OFG	−82.29	28.23	0.25	−0.40*
R. middle OFG	−38.72	26.54	0.03	−0.20

PAI, personality assessment inventory; OFG, orbital frontal gyrus; SE, standard error.
*Bonferroni-corrected $P < 0.01$.

medial PFC cluster and all three subscores of the PAI paranoia scale (hypervigilance: $r = -0.44$, $P < 0.017$; persecution: $r = -0.40$, $P < 0.017$; resentment: $r = -0.37$, $P < 0.005$).

Finally, it was conceivable that even subclinical psychopathology or level of education could have affected the subjective estimates of how much sleep was needed before experiencing impairments. Therefore, to address this possibility, we correlated scores on each of the hypothesized PAI scales and education (in years) with the minimum amount of sleep reported before noticeable impairment. Sleep need was not related significantly to depression ($r = 0.22$, $P = 0.11$), somatization ($r = 0.11$, $P = 0.43$) or anxiety ($r = 0.17$, $P = 0.21$), but was related to level of paranoia ($r = 0.34$, $P = 0.01$). Subjective minimum sleep need before the emergence of noticeable work impairment was correlated negatively with years of education ($r = -0.30$, $P = 0.02$). This suggests that higher education level was associated generally with a lower perceived sleep need.

DISCUSSION

Habitual sleep in excess of perceived minimal need to avoid impairment, defined here as 'sleep credit', was associated with greater grey matter volume of the medial frontal and orbitofrontal cortex, regions important to emotional perception and affective regulation. Furthermore, individual variation in grey matter volume of the medial prefrontal cortex cluster was associated with global self-perceived emotional intelligence, in particular capacities involving interpersonal skills that contribute to the ability to understand and relate well with others. Similarly, greater grey matter volume of the same cluster was correlated with reduced severity on several indices of psychopathology, particularly in terms of overall somatic complaints, depression and paranoia. In short, sleeping more than the minimum required to sustain performance was associated with increased grey matter volume in cortical areas critical to emotional regulation, and larger volume of these areas was associated with better emotional and psychological health.

Our data offer additional support to a line of converging empirical studies showing that function, structure and connectivity of medial prefrontal and orbitofrontal cortices are vital to the understanding of sleep and its relationship to behaviour. For example, decreased metabolic activity following one night of sleep deprivation was not restricted to, but predominant within, this brain region, particularly within the bilateral gyrus rectus (Thomas *et al.*, 2000). Furthermore, attentional lapses appear to be linked to diminished activity in the medial prefrontal cortex (Chee *et al.*, 2008). Volumetric data also point to an important connection between the medial prefrontal cortex and sleep-related problems. For instance, grey matter volume in the context of both sleep disorders and increased daytime sleepiness in healthy adults tends to be reduced in this region in association with greater sleep-related pathology (Altena *et al.*, 2010; Joo *et al.*, 2009; Killgore *et al.*, 2012b; Morrell, 2003). Lastly, functional connectivity of the medial prefrontal cortex with other emotional and socially relevant brain regions has been shown to be correlated inversely with sleep duration (Killgore *et al.*, 2012a) or is particularly weakened following a full night of sleep deprivation (Yoo *et al.*, 2007). Our data complement these findings by showing that grey matter structure within the medial prefrontal cortex varies systematically with habitual 'sleep credit'.

The present study also builds upon and extends previous research into the beneficial effects of excess (Anderson *et al.*, 2009) or 'banked' sleep (Rupp *et al.*, 2009a,b). Previously, it was shown that 'banking sleep' for 1 week was associated with greater resilience to, and better recovery

from, a period of insufficient sleep (Rupp *et al*., 2009a,b). In these studies, 'banking sleep' was conceptualized as getting more than habitual sleep (e.g. 10 h time in bed instead of an individual's typical 8 h). The authors argued that sleep history needs careful consideration in experimental sleep deprivation studies due to its potential moderating effect, and that one night of baseline sleep might not provide a sufficient baseline measure. Our data suggest habitual 'sleep credit' - that is, sleeping more than needed subjectively (e.g. getting 8 h if one perceives 5 h to be the point at which an impairment would be noticed) - as an additional putative moderator of the sleep–behaviour relationship. We showed that sleeping more than needed subjectively was associated with greater grey matter volume within the medial prefrontal cortex, a brain region that has been implicated strongly in sleep, sleep deprivation and their behavioural correlates. While the cross-sectional nature of our data do not allow us to draw conclusions regarding the direction of this effect, it allows us to pose the question of whether individuals who habitually sleep more than their subjective need might also be more resistant to acute sleep deprivation – possibly because of an advantageous neuronal substrate. Future studies employing longitudinal assessment, neuroimaging and acute sleep deprivation may be able to address this possibility.

Probably very few would contest that surplus sleep provides a range of benefits. Our data showed that sleeping in excess of the amount needed subjectively to avert degraded performance was linked to greater grey matter volume in a cortical region critical to both cognition and emotion (Fuster, 2008). Thus, in additional to highlighting the neurostructural benefits associated with 'sleep credit', our data replicated previous findings of behavioural deficits associated with insufficient sleep, particularly in terms of complex cognition such as emotional intelligence and psychological health (Kahn-Greene *et al*., 2007; Killgore *et al*., 2008). In those previous studies, prolonged sleep deprivation led to a degradation of both global and specific aspects of emotional intelligence, whereas psychopathological symptoms, including somatization, anxiety, depression and paranoia, increased without sleep. Our data showed that most of these same symptom dimensions, including somatization, depression and paranoia, were correlated with grey matter volume of the medial prefrontal cortex cluster, the very region that was implicated in habitually sleeping longer than needed subjectively. Longitudinal data are needed to establish whether habitual 'sleep credit' in fact induces grey matter changes in this region or whether these cortical volume differences reflect a biological substrate permitting decreased sleep need.

One previous study investigated whether the difference between habitual sleep duration and perceived sleep need was associated with a variety of sleep and trait measures such as sleep propensity, subjective daytime sleepiness, psychomotor vigilance, anxiety and personality (Anderson *et al*., 2009). Interestingly, no difference emerged in these putative behavioural correlates of 'sleep credit' (i.e. getting more sleep than needed), sleep deficit (i.e. getting less sleep than needed) and getting as much sleep as needed. However, neurostructural and higher-cognitive correlates such as emotional intelligence were not investigated, and the accumulated 'sleep credit' in our sample was, on average, greater than in the Anderson *et al.* (2009) study, suggesting limited comparability between studies. Future research should investigate whether 'sleep credit' contributes to elementary cognitive functions such as psychomotor vigilance, as well as higher-order cognitive processes such as emotional intelligence to resolve this apparent discrepancy.

Finally, although our primary hypotheses were restricted to four PAI subscales (i.e. somatization, depression, anxiety, paranoia), as previous research has shown sleep deprivation to affect these scales specifically (Kahn-Greene *et al*., 2007), we also conducted additional exploratory analyses. For comprehensiveness and to obviate any bias in reporting, we conducted multiple regressions with the remaining non-hypothesized PAI subscales (i.e. anxiety-related disorders, mania, schizophrenia, borderline features, antisocial features) at a Bonferroni-corrected threshold of $P < 0.05$. Interestingly, the specificity of the association between sleep deprivation and PAI psychopathology demonstrated by Kahn-Greene *et al.* (2007) was also observed in the present study of 'sleep credit'. Specifically, after correction for multiple comparisons, grey matter volume did not relate to any of these scales except for schizophrenia, which showed a negative association with grey matter volume within the left gyrus rectus, superior and medial OFG only (Table S1). We also found that formal education level was correlated negatively with the perceived amount of sleep necessary before functional work impairments become noticeable. While not hypothesized, this negative relationship suggests that individuals with higher educational attainment perceive themselves as able to function with less sleep before experiencing impaired performance. There are several possible explanations for this relationship, including greater cognitive ability among those with higher educational attainment, which might confer greater cognitive reserve, or individuals with lower education may have been less reliable in reporting their sleep need and impairment levels. These questions were not addressed directly in the present study and will require additional research.

The study is not without limitations and our results need to be replicated, preferably in a larger independent sample with prospective objective measurement of actual sleep via actigraphy or some method of ambulatory monitoring (Anderson *et al*., 2009). Despite including 55 healthy adults, our sample size was still at the lower end of the ideal number of subjects to be included in a multiple regression analysis with two predictors. Also, whereas most regression diagnostics (i.e. standardized residuals, Durban–Watson test statistic, collinearity statistic, Cook's distance, Mahalanobis distance, covariance ratio) did not reveal any violation of multiple regression assumptions for any of the variables of interest, hat values exceeded common thresholds on PAI scales of

somatization, anxiety and depression for a few selected subjects, suggesting possible excess leverage effects. We therefore cannot readily generalize results regarding these three variables beyond our sample. Additionally, our definition of 'sleep credit' is not unassailable. Here, we defined 'sleep credit' as the amount of sleep that an individual obtains habitually relative to that person's own subjectively perceived sleep need, defined as the threshold of sleep necessary before daytime impairment is noted. Alternatively, 'sleep credit' could be defined in relation to subjective sleep necessary for optimal performance in daily life. While conceptually similar and potentially related, 'lack of impairment' and 'optimal functioning' are clearly distinct constructs that may be affected differentially by sleep loss. It is likely that the behavioural and brain structural correlates of excess sleep beyond an 'optimal functioning' threshold would be different to those explored here examining excess sleep beyond a 'no impairment' threshold. Teasing apart the role of sleep and brain structure on each of these deserves further study. It remains to be shown whether and how differences in operationalization of 'sleep credit' might influence findings of grey matter correlates and their association with emotional intelligence and mental health. Future investigations should also include a more detailed assessment of the type of impairment (e.g. worse memory, difficulties in concentration, changes in emotional response and expression) that is noticed when sleep is less than subjective need, including daytime sleepiness (Killgore *et al*., 2012b). Also of interest might be an assessment of each participant's specific work situation and job requirements to determine whether the effects of 'sleep credit' might depend upon such work-setting factors. Furthermore, it may be useful to explore the reasons why some participants habitually obtain the sleep they need subjectively while others do not. Lastly, readers should bear in mind that these data are correlational, and therefore causality cannot be inferred.

In conclusion, this is the first voxel-based morphometric study to show that sleeping in excess of subjective minimal need is associated significantly with greater grey matter volume within the medial prefrontal cortex, a region critical to the monitoring and control of affective processes. Notably, the volume of this same region was correlated independently with greater emotional intelligence and lower scores on indices of psychopathology in the same participants. These data support the notion that sleeping beyond the minimal subjective requirements for adequate performance may affect brain structure and relevant emotional capacities.

ACKNOWLEDGEMENTS

This research was supported by a USAMRAA grant (W81XWH-09-1-0730).

CONFLICTS OF INTEREST

No conflicts of interests declared.

REFERENCES

Altena, E., Vrenken, H., Van Der Werf, Y. D., van den Heuvel, O. A. and Van Someren, E. J. W. Reduced orbitofrontal and parietal gray matter in chronic insomnia: a voxel-based morphometric study. *Biol. Psychiatry*, 2010, 67: 182–185.

Anderson, C., Platten, C. R. and Horne, J. A. Self-reported 'sleep deficit' is unrelated to daytime sleepiness. *Physiol. Behav.*, 2009, 96: 513–517.

Banks, S. and Dinges, D. F. Behavioral and physiological consequences of sleep restriction. *J. Clin. Sleep Med.*, 2007, 3: 519–528.

Bar-On, R. *BarOn Emotional Quotient Inventory: A Measure of Emotional Intelligence—Technical Manual*. Multi-Health Systems, North Tonawanda, NY, 2006.

Chee, M. W. L., Tan, J. C., Zheng, H. *et al.* Lapsing during sleep deprivation is associated with distributed changes in brain activation. *J. Neurosci.*, 2008, 21: 5519–5528.

Cirelli, C., Shaw, P. J., Rechtschaffen, A. and Tononi, G. No evidence of brain cell degeneration after long-term sleep deprivation in rats. *Brain Res.*, 1999, 840: 184–193.

Ferrara, M. How much sleep do we need? *Sleep Med. Rev.*, 2001, 5: 155–179.

Fuster, J. M. *The Prefrontal Cortex*, 4th edn. Academic Press, London, 2008.

Gao, B. B., Cam, E. E., Jaeger, H. H., Zunzunegui, C. C., Sarnthein, J. J. and Bassetti, C. L. C. Sleep disruption aggravates focal cerebral ischemia in the rat. *Sleep*, 2010, 33: 879–887.

Joo, E. Y., Tae, W. S., Kim, S. T. and Hong, S. B. Gray matter concentration abnormality in brains of narcolepsy patients. *Korean J. Radiol.*, 2009, 10: 552–558.

Joo, E. Y., Tae, W. S., Lee, M. J. *et al.* Reduced brain gray matter concentration in patients with obstructive sleep apnea syndrome. *Sleep*, 2010, 33: 235–241.

Kahn-Greene, E. T., Killgore, D. B., Kamimori, G. H., Balkin, T. J. and Killgore, W. D. S. The effects of sleep deprivation on symptoms of psychopathology in healthy adults. *Sleep Med.*, 2007, 8: 215–221.

Killgore, W. D. S., Kahn-Greene, E. T., Lipizzi, E. L., Newman, R. A., Kamimori, G. H. and Balkin, T. J. Sleep deprivation reduces perceived emotional intelligence and constructive thinking skills. *Sleep Med.*, 2008, 9: 517–526.

Killgore, W. D. S., Schwab, Z. J. and Weiner, M. R. Self-reported nocturnal sleep duration is associated with next-day resting state functional connectivity. *Neuroreport*, 2012a, 23: 741–745.

Killgore, W. D. S., Schwab, Z. J., Kipman, M., DelDonno, S. R. and Weber, M. Voxel-based morphometric gray matter correlates of daytime sleepiness. *Neurosci. Lett.*, 2012b, 518: 10–13.

Morey, L. C. *Personality Assessment Inventory*. Psychological Assessment Resources Inc., Lutz, FL, 1991.

Morrell, M. Changes in brain morphology associated with obstructive sleep apnea. *Sleep Med.*, 2003, 4: 451–454.

Mueller, A. D., Mear, R. J. and Mistlberger, R. E. Inhibition of hippocampal neurogenesis by sleep deprivation is independent of circadian disruption and melatonin suppression. *Neuroscience*, 2011, 193: 170–181.

National Sleep Foundation. 2005 Sleep in America Poll. Available at: http://www.sleepfoundation.org (accessed 2 November 2012).

Novati, A., Hulshof, H. J., Koolhaas, J. M., Lucassen, P. J. and Meerlo, P. Chronic sleep restriction causes a decrease in hippocampal volume in adolescent rats, which is not explained by changes in glucocorticoid levels or neurogenesis. *Neuroscience*, 2011, 190: 145–155.

O'Donoghue, F. J. Cerebral structural changes in severe obstructive sleep apnea. *Am. J. Respir. Crit. Care Med.*, 2005, 171: 1185–1190.

Punjabi, N. M., Bandeen-Roche, K. and Young, T. Predictors of objective sleep tendency in the general population. *Sleep*, 2003, 26: 678–683.

Rupp, T. L., Wesensten, N. J. and Balkin, T. J. Sleep history affects task acquisition during subsequent sleep restriction and recovery. *J. Sleep Res*., 2009a, 19: 289–297.

Rupp, T. L., Wesensten, N. J., Bliese, P. D. and Balkin, T. J. Banking sleep: realization of benefits during subsequent sleep restriction and recovery. *Sleep*, 2009b, 32: 311–321.

Thomas, M., Sing, H., Belenky, G. *et al.* Neural basis of alertness and cognitive performance impairments during sleepiness. I. Effects of 24 h of sleep deprivation on waking human regional brain activity. *J. Sleep Res*., 2000, 9: 335–352.

Van Dongen, H. and Maislin, G. The cumulative cost of additional wakefulness: dose–response effects on neurobehavioral functions and sleep physiology from chronic sleep restriction and total sleep deprivation. *Sleep*, 2003, 26: 117–126.

Yoo, S. S., Gujar, N., Hu, P., Jolesz, F. A. and Walker, M. P. The human emotional brain without sleep—a prefrontal amygdala disconnect. *Curr. Biol*., 2007, 17: R887–R878.

Zunzunegui, C. C., Gao, B. B., Cam, E. E., Hodor, A. and Bassetti, C. L. C. T-O-131 Sleep disturbance impairs stroke recovery in the rat. *Sleep*, 2011, 34: 1261–1269.

SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Table S1. Stepwise linear regression of grey matter volume correlates of non-hypothesized PAI psychopathology.

Self-Reported Sleep Correlates with Prefrontal-Amygdala Functional Connectivity and Emotional Functioning

William D. S. Killgore[1,2]

[1]McLean Hospital, Belmont, MA

[2]Harvard Medical School, Boston, MA

Address correspondence and reprint requests to William D. "Scott" Killgore, Ph.D., Center for Depression, Anxiety, and Stress Research, McLean Hospital, Harvard Medical School, 115 Mill Street, Belmont, MA 02478, or e-mail (killgore@mclean.harvard.edu).

Abstract

Study Objectives: Prior research suggests that sleep deprivation is associated with declines in some aspects of emotional intelligence and increased severity on indices of psychological disturbance. Sleep deprivation is also associated with reduced prefrontal-amygdala functional connectivity, potentially reflecting impaired top-down modulation of emotion. It remains unknown whether this modified connectivity may be observed in relation to more typical levels of sleep curtailment. We examined whether self-reported sleep duration the night before an assessment would be associated with these effects.

Design: Participants documented their hours of sleep from the previous night, completed the Bar-On Emotional Quotient Inventory (EQ-i), Mayer-Salovey-Caruso Emotional Intelligence Test (MSCEIT), Personality Assessment Inventory (PAI), and underwent resting-state functional magnetic resonance imaging (fMRI).

Setting: Outpatient neuroimaging center at a private psychiatric hospital.

Participants: Sixty-five healthy adults (33 men, 32 women), ranging in age from 18-45 years.

Interventions: N/A

Measurements and Results: Greater self-reported sleep the preceding night was associated with higher scores on all scales of the EQ-i but not the MSCEIT, and with lower symptom severity scores on half of the psychopathology scales of the PAI. Longer sleep was also associated with stronger negative functional connectivity between the right ventromedial prefrontal cortex and amygdala. Moreover, greater negative connectivity between these regions was associated with higher EQ-i and lower symptom severity on the PAI.

Conclusions: Self-reported sleep duration from the preceding night was significantly correlated with negative prefrontal-amygdala connectivity, perceived emotional intelligence, and the severity of subjective psychological distress. More sleep was associated with higher emotional and psychological strength.

Sleep loss has a profound effect on elementary cognitive processes such as simple alertness, psychomotor vigilance, and response speed [1, 2]. However, there is now a growing literature suggesting that sleep loss also has significant effects on mood and emotional functioning [3-6]. Sleep deprivation increases physiological reactivity in response to emotional stressors [7], reduces the psychological threshold for coping with stress [8], and even leads to poorer frustration tolerance and an altered perception of the motives of others [9]. Sleep deprivation impairs emotionally based decision-making [10] and the ability to use emotions to effectively guide moral judgment [11-13]. Moreover, extended sleep deprivation is associated with significant declines on standardized measures of coping skills and emotional intelligence (EI), a set of capabilities and traits that involve the ability to understand and regulate emotions [14]. In one study, sleep deprivation was associated with significant declines in the ability to understand emotional responses in others and led to reduced self-reported interpersonal skills, including degraded empathy, stress management capacities, and impulse control [14]. Even in healthy individuals, prolonged sleep deprivation leads to significant worsening on several standardized indices of psychopathology, including scales measuring somatic complaints, anxiety, depression, and paranoia [15]. In short, when sleep is lacking, affective functioning becomes poorly regulated and emotionally salient stimuli may have a greater influence over cognitive processes.

While the causal mechanisms for these mood and emotional changes are poorly understood, some evidence suggests that they may emerge from measurable alterations in brain functioning that occur following insufficient sleep or total sleep deprivation. Early brain imaging studies suggested that sleep deprivation is associated with significant

declines in global cerebral energy metabolism [16]. These declines are particularly notable within the prefrontal cortex, including the ventromedial regions [16], which are important to emotional regulation and behavioral control [17, 18]. More recent studies using functional magnetic resonance imaging (fMRI) suggest that the increased emotional responsiveness during sleep deprivation may be due in part to changes in the strength of functional connectivity between the emotional regulating regions of the medial prefrontal cortex and the amygdala, a structure involved in triggering emotional responses to salient stimuli [19]. Other evidence suggests that this modified connectivity between the emotional regulation and emotional responsive regions of the brain may contribute to altered responsiveness to both positive and negatively valenced stimuli under conditions of sleep deprivation [20]. Speculatively, such an alteration in the functional balance between these regions may affect higher order regulation of emotional processes, which could conceivably be observed as declines in EI and even the emergence of symptoms of psychopathology.

While the effects of total sleep deprivation on EI capacities and symptoms of psychopathology have been well documented within the confines of highly controlled laboratory environments [14, 15], virtually no information exists regarding the relation between typical nightly sleep duration in the natural home environment and changes in emotional capacities. A recent fMRI study by our group demonstrated that self-reported sleep duration was reliably associated with next-day resting-state functional connectivity within the brain's default mode network, which includes regions of the medial prefrontal cortex and posterior cingulate cortex [21]. It is, therefore, possible that subtle reductions in nocturnal sleep, even well within the normal range obtained by most healthy individuals on any given night, may be sufficient enough to be associated with variations in EI and

psychopathology. Accordingly, we collected self-report information regarding typical and recent sleep patterns as well as standardized indices of EI and psychopathology in a sample of healthy participants. Based on our prior findings of changes in EI and psychopathology during total sleep deprivation, and other work showing altered prefrontal – amygdala connectivity under similar conditions, we hypothesized that 1) greater amounts of sleep reported for the night before an assessment would correlate with higher scores on measures of EI and lower scores on indices of psychopathology, 2) more sleep would be associated with increased negative functional connectivity between the ventromedial prefrontal cortex (vmPFC) and amygdala (i.e., suggesting a negative relationship between the intrinsic activation patterns of the amygdala and vmPFC in rested individuals), and 3) the strength of this negative functional connectivity would be directly related to higher EI and lower psychopathology scores in healthy adults.

Method

Participants

Sixty-five healthy adults (33 men, 32 women), ranging in age from 18-45 years (M = 30.2; SD = 8.0) were recruited via internet advertisements and flyers from the vicinity of the Boston metropolitan area. Participants were screened via telephone interview using standard psychiatric diagnostic criteria [22], and deemed to be free from any history of serious medical illnesses, including neurological, Axis I psychiatric, or substance use disorders (including alcohol and illicit drugs), or evidence of clinically significant sleep disorders. All 65 participants provided complete data for the questionnaires. A subsample (n = 58) of this group (29 men, 29 women), ranging in age from 18-45 (M = 30.5; SD = 8.0) also provided usable resting state fMRI data that were

correlated with the questionnaire data. All participants provided written informed consent and were compensated for their time. This research protocol was reviewed and approved by the Institutional Review Board of McLean Hospital.

Materials and Procedure

Sleep Questionnaires. Participants arrived at the laboratory between 0900 and 1100 in the morning. Upon arrival, each participant completed a brief questionnaire about their recent sleep schedule and typical habits. The primary question of interest simply asked participants: "How much sleep did you get last night?" This variable, identified as *Sleep Last Night*, was scored in hours. The questionnaire also included queries about typical bedtimes and wakeup times for weekdays and weekends. Based on this information an estimated *Sleep Debt* variable was also computed by subtracting a weighted average of typical sleep on weekdays and weekends from the *Sleep Last Night* variable. Additionally, participants also reported whether they had problems falling or staying asleep as a simple index of insomnia complaints. Participants also completed the Morningness-Eveningness Questionnaire (MEQ)[23]. Higher scores on the MEQ indicate a preference for earlier rise and bed times and a tendency to function most effectively earlier in the day.

Emotional Intelligence Scales. Participants completed two normed, well-validated, and commercially available measures of EI. As a mixed model, or *Trait* measure of EI, participants completed the Bar-On Emotional Quotient Inventory (EQ-i)[24]. A 125-item self-report measure, the EQ-i provides a global score of EI (*Total EQ*), as well as five composite subscales measuring various self-perceived facets of the construct, including the ability to relate well with others (*Interpersonal*), emotional self-awareness

and self-confidence (*Intrapersonal*), emotional flexibility and problem solving (*Adaptability*), ability to cope with stress (*Stress Management*), and general optimism and contentedness (*General Mood*). The raw EQ-i scores were transformed into standard scores based on the general population norms provided by the test manual and scoring program [24]. We also tested *Ability* Emotional Intelligence using the Mayer-Salovey-Caruso Emotional Intelligence Test (MSCEIT)[25], a performance based test of the capacity to reason about and solve emotional problems. This test yields a *Total EI* score, as well as two Area scores. The first Area score measures the ability to perceive emotions and use that information to facilitate thought (*Experiential EI*), and is comprised of two branch scores known as *Perceiving* and *Facilitating* emotions. The second Area score measures the ability to understand and control emotions (*Strategic EI*), and is comprised of two branch scores known as *Understanding* and *Managing* emotions. Raw MSCEIT scores were transformed into standardized scores based on the general consensus scoring method (as opposed to expert consensus method) described in the test manual [25]. Based on our prior published findings [14], we specifically hypothesized that greater sleep and increased functional connectivity variables would correlate with *Total EQ*, *Intrapersonal*, *Interpersonal*, and *Stress Management* variables from the EQ-i.

Psychopathology Scale. As a measure of psychopathologic symptom severity, participants completed the Personality Assessment Inventory (PAI), an objective measure that includes 344 statements that are self-rated on a 4-point Likert scale [26]. The PAI includes 18 primary scales: *Somatic Complaints* (SOM), which measures concerns about health and physical functioning; *Anxiety* (ANX), which measures general tension and negative affect; *Anxiety Related Disorders* (ARD), which assesses symptoms related to

specific anxiety disorders; *Depression* (DEP), which measures common cognitive, affective, and physiological symptoms of depression; *Mania* (MAN), which measures common clinical features of hypomania and mania; *Paranoia* (PAR), which assesses paranoid features such as hypervigilance, resentment, and feelings of persecution; *Schizophrenia* (SCZ), which measures a variety of symptoms including unusual beliefs and perceptions, social deficits, and attentional problems; *Borderline Features* (BOR), which assesses broad problems with interpersonal functioning; *Antisocial Features* (ANT), which taps into constructs of advensturesomeness, egocentricity, lack of empathy, and antisocial attitudes; *Alcohol Problems* (ALC), which assesses behaviors and consequences associated with alcohol abuse and dependence; *Drug Problems* (DRG), which measures attitudes and behaviors related to drug abuse and dependence; *Suicidal Ideation* (SUI), which assesses thought content related to death and suicide; *Stress* (STR), which provides an index of current life stressors; *Nonsupport* (NON), which measures the perception of unavailability of social support; *Treatment Rejection* (RXR), which assesses a tendency to be satisfied with the current status quo and a disinterest in or unwillingness to participate in therapy; *Dominance* (DOM), an interpersonal scale which measures a bipolar dimension of dominance (versus submissiveness); *Warmth* (WRM), an interpersonal scale which measures a bipolar dimension of empathy (versus rejecting). Raw scores on the PAI were transformed to standardized T-scores based on a normative sample of 1000 community-dwelling adults as described in the test manual [26]. According to prior published findings [15], we specifically hypothesized that greater sleep and increased functional connectivity variables would correlate with *SOM, ANX, DEP, and PAR* variables from the PAI.

Neuroimaging. Participants underwent a 6-minute, eyes open, resting state functional magnetic resonance imaging scan (fMRI) between 1300 and 1500 in the afternoon. Due to the nature of the resting state scan (i.e., non-task engagement—mind wandering), we did not ask the participants to engage in any sort of vigilance control task during this data collection. Images were collected on a 3T Siemens Tim Trio scanner (Erlangen, Germany), fitted with a 12-channel head coil. Standard structural images were acquired first for use in spatial normalization and for removal of tissue confounds. These images comprised a T1-wighted 3D MPRAGE sequence (TR/ TE/ flip angle = 2.1s/2.25ms/12°), which yielded 128 sagittal slices (256x256 matrix) with a slice thickness of 1.33mm and a voxel size of 1.33x1x1mm. For the resting state scan, 180 images were collected (3.5 mm thickness, no skip; 22.4 cm field of view; 64 x 64 acquisition matrix) over 34 transverse interleaved slices using a T2*-weighted blood oxygen level dependent (BOLD) echoplanar imaging (EPI) sequence (TR /TE / flip angle = 2.0s/30ms/90°).

Image Processing. Resting state data were preprocessed using standard algorithms in SPM8, including motion correction, slice-timing correction, anatomical co-registration, spatial normalization, and spatial smoothing (full width at maximum [FWHM] = 6 mm). Voxels were resliced to 2x2x2 mm. The time series of resting state data was analyzed using the Functional Connectivity (CONN) Toolbox [27] version 13i (http://www.nitrc.org/projects/conn). As part of this process, the data were band-pass filtered (0.008, 0.10 Hz), and corrected for physiological noise using the *aCompCor* strategy [28]. Major confounders were removed using principle components analysis to control for the effects of white matter and cerebrospinal fluid, and motion parameters

were included as nuisance covariates; the resultant residual BOLD time series was used for subsequent functional connectivity analyses. To examine functional connectivity, four regions of interest (ROIs) were placed (vmPFC seed regions = left and right gyrus rectus; target regions = left [220 voxels] and right [248 voxels] amygdala) using the Automated Anatomical Labeling (AAL) Atlas [29]. The gyrus rectus was selected based on recent work suggesting that gray matter of this region is associated with EI traits [30] as well as sleep-related problems [31, 32].

Data Analysis

Questionnaires. Sleep variables from the questionnaires were evaluated for bivariate intercorrelations. Further, based on a tercile division of self-reported sleep (*Sleep Last Night*), participants were initially divided into three groups of Low (≤ 6.5 hours, $n = 22$), Moderate (6.6 – 7.9 hours, $n = 21$), or High (≥ 8 hours, $n = 22$) sleep per night. Initial analyses were conducted using one-way analysis of variance to determine whether groups differed significantly on the primary EI and psychopathology variables. Secondary analyses were then undertaken using Pearson correlations to more closely examine the association between the sleep questionnaire item, *Sleep Last Night*, and scores on the primary and subscale scores of the EQ-i, MSCEIT, and PAI. Significance was evaluated at $p < .05$. Due to the large number of correlations, the p-values were adjusted using a Bonferroni correction for all non-hypothesized associations within each analysis set.

Resting State Connectivity. Within the CONN Toolbox, the mean BOLD time series from the resting state scan was calculated for all voxels within the two seed regions for each subject. As a measure of functional connectivity, the zero-lagged bivariate

correlation was calculated between the mean time course of each vmPFC seed region and every other voxel in the brain on a subject-by-subject basis. To improve normality before entry into the second level random effects general linear model, all bivariate correlation maps were Fisher transformed (i.e., z-score transformed) via an inverse hyperbolic tangent function [27]. Each participant's self reported sleep was then regressed against these individual beta maps to determine the correlation between functional connectivity and sleep. We corrected for all voxels in the bilateral amygdala ROI with a height threshold of $p < .05$ (FWE-corrected), while spatial extent (i.e., minimum cluster size) was set at 10 voxels. The mean of the beta values from the resulting cluster was extracted for each individual and correlated with the indices of emotional intelligence and psychopathology.

Results

Questionnaires

Sleep Last Night. As evident in Table 1, participants reported obtaining an average of 6.97 hours (*SD* = 1.07) the night before the assessment session. Hours of reported sleep ranged from 4.0 to 9.0. From questions pertaining to estimated weekday and weekend sleep, participants reported generally sleeping 7.43 (SD = 0.79) hours per night on average. These data were used to calculate an index of estimated *Sleep Debt*, which suggested that participants had reduced their sleep by approximately 26 minutes on the night preceding the scan compared to their typical sleep (see Table 1). *Sleep Last Night* was not correlated with age, MEQ, or typical bed/wakeup times. As might be

expected, however, MEQ was strongly correlated with typical bedtimes and wakeup times.

INSERT TABLE 1 ABOUT HERE

For preliminary analysis, *Sleep Last Night* was divided into three categories of Low (≤ 6.5 hours), Moderate (6.6 – 7.9 hours), or High (≥ 8 hours). When divided in this manner, 22 participants were in the Low sleep (M = 5.75 hours, SD = 0.75), 21 were in the Moderate sleep (M = 7.09 hours, SD = 0.20), and 22 were in the High sleep (M = 8.08 hours, SD = 0.23) groups. Because age is sometimes associated with sleep duration, this relationship was examined in the current dataset. However, age was not correlated with *Sleep Last Night* (r = -.02, p = .88), so it was not included as a covariate in subsequent analyses. Finally, 43.8% of the sample (n = 28) reported that they occasionally had insomnia complaints (i.e., difficulty falling asleep or staying asleep). This variable was included as a nuisance covariate in subsequent partial correlation analyses involving emotional intelligence and psychopathology measures.

Emotional Intelligence. As evident in Figure 1A, there was a main effect of sleep category for Total EQ-i scores, $F(2,62) = 3.64$, p = .032, suggesting that a greater amount of sleep the preceding night was associated with higher Total EQ. Tukey post-hoc tests showed that this effect was driven primarily by significantly higher EQ scores for the High versus Low sleep group ($p < .05$). As shown in Figure 2, the number of hours of *Sleep Last Night* was significantly correlated with higher scores for *Total EQ* (r = .396, p = .001), and all 5 composite EQ-i subscale scores, including *Intrapersonal* (r = .291, p =

.019), *Interpersonal* (r = .299, p = .015), *Stress Management* (r = .362, p = .003), *Adaptability* (r = .392, p = .001; Bonferroni Corrected p = .009), and *General Mood* (r = .300, p = .015; Bonferroni Corrected p = .135), suggesting that more sleep was linearly associated with higher EQ-i scores. In contrast, MSCEIT scores did not differ significantly across sleep duration categories (see Figure 1B), and none of the scales of the MSCEIT were significantly correlated with hours of *Sleep Last Night* (see Figure 2), (all rs < .14, all *p-values* > .30). To address possible concern that this difference between the strength of correlations on the two scales might be accounted for by response biases affecting the self-report measures, the same analyses were conducted for the self-report scales using partial correlations to control for scores on the *Negative Impression Index* of the EQ-i (i.e., the tendency to "fake bad"). For the EQ-i, four of the six partial correlations remained significant after controlling for response bias, including *Total EQ* (r = .301, p = .015), *Intrapersonal* (r = .185, p = .142), *Interpersonal* (r = .272, p = .030), *Stress Management* (r = .306, p = .014), *Adaptability* (r = .297, p = .017; Bonferroni Corrected p = .034), and *General Mood* (r = .239, p = .057; Bonferroni Corrected p = .114). Finally, we explored the potential effect of insomnia complaints on these associations. Figure 2 shows that statistically controlling for insomnia complaints modestly reduced the strength of the correlations, although *Total EQ* and *Adaptability* remained significantly correlated with *Sleep Last Night* even after removing the influence of insomnia problems.

INSERT FIGURE 1 ABOUT HERE

INSERT FIGURE 2 ABOUT HERE

Psychopathology. Linear associations were also obtained among several variables of the PAI with *Sleep Last Night* (see Figure 3). Obtaining more hours of *Sleep Last Night* correlated with significantly lower scores for *ANX* (r = -.344, p = .007), *ARD* (r = -.302, p = .018; Bonferroni Corrected p = .252), *DEP* (r = -.378, p = .003), *PAR* (r = -.385, p = .002), *SCZ* (r = -.385, p = .002; Bonferroni Corrected p = .028), *ANT* (r = -.284, p = .027; Bonferroni Corrected p = .378), *ALC* (r = -.263, p = .040; Bonferroni Corrected p = .56), *STR* (r = -.355, p = .005; Bonferroni Corrected p = .07), and higher scores for *RXR* (r = .268, p = .037; Bonferroni Corrected p = .518). In contrast, Sleep Last Night was not significantly correlated with scores for *SOM*, *MAN*, *BOR*, *DRG*, *AGG*, *SUI*, *NON*, *DOM*, and *WRM* (all $rs < |.22|$, all *p-values* > .09). Figure 3 also shows that statistically controlling for insomnia complaints had only minimal effects on the strength of most correlations between *Sleep Last Night* and PAI variables.

INSERT FIGURE 3 ABOUT HERE

Neuroimaging

VMPFC – Amygdala Functional Connectivity. Whole brain connectivity maps through an axial slice showing the vmPFC and amygdala are displayed in Figure 4. These maps are corrected for multiple comparisons using FWE at $p < .05$ for the whole brain. From these maps, initial connectivity values (Fisher transformed correlation

coefficients) were extracted for the left and right amygdala ROIs for all voxels exceeding the corrected threshold and are presented in Table 2.

INSERT FIGURE 4 ABOUT HERE

INSERT TABLE 2 ABOUT HERE

Functional connectivity between the left vmPFC seed region and voxels within either the right or left amygdala was not significantly correlated with *Sleep Last Night*. In contrast, greater *Sleep Last Night* was associated with greater negative functional connectivity between the right vmPFC seed region and voxels within the right amygdala (see Figure 5). This analysis yielded a cluster of 10 voxels in the right amygdala ROI [MNI coordinates: x = 24, y = 2, z = -22]. Connectivity was negatively correlated with greater self-reported sleep time (T = 4.20, r = -.49). Age was not associated with connectivity strength (r = -.009, p = .94), so it was not included as a covariate in the analysis.

INSERT FIGURE 5 ABOUT HERE

Neuroimaging and Questionnaire Correlates

Connectivity Strength and EI. The beta values from the right amygdala cluster representing the strength of connectivity with the vmPFC that covaried with *Sleep Last*

Night were extracted and entered into a correlation analysis with the various EI indices. As shown in Figure 6, the strength of the negative functional connectivity between the right vmPFC and right amygdala was linearly correlated with three EI measures, including *Total EQ* (r = -.287, p = .029), *Stress Management* (r = -.276, p = .036), and *Adaptability* (r = -.305, p = .020; Bonferroni Corrected p = .18). These findings suggest that greater negative connectivity between these regions was associated with higher EI scores on these scales, but not to the *Intrapersonal*, *Interpersonal*, or *General Mood* scales (all *rs* < |.34|, all *p-values* > .07). In contrast, the strength of connectivity between the right vmPFC and amygdala was unrelated to any of the scores on the MSCEIT, including *Total EI*, *Experiential EI*, *Strategic EI*, *Perceiving EI*, *Facilitating EI*, *Understanding EI*, *Managing EI* (all *rs* < |.16|, all *p-values* > .25). Figure 6 also shows that once insomnia complaints were statistically controlled, the strength of the correlation between EI scales and connectivity was reduced and none of the findings reached significance.

INSERT FIGURE 6 ABOUT HERE

Connectivity Strength and Psychopathology. The extracted vmPFC-amygdala connectivity data were also correlated with the indices of psychopathology from the PAI. As evident in Figure 7, greater positive connectivity was associated increased scores for *ANX* (r = .325, p = .013), *ARD* (r =.306, p = .021; Bonferroni Corrected p = .294), *DEP* (r =.388, p = .003), *PAR* (r = .286, p = .031), *SCZ* (r = .305, p = .021; Bonferroni Corrected p = .294), *BOR* (r = .335, p = .011; Bonferroni Corrected p = .154), SUI (r =

.368, p = .005; Bonferroni Corrected p = .070), STR (r = .339, p = .010; Bonferroni Corrected p = .140). In contrast, greater negative connectivity between vmPFC and amygdala was associated with healthier scores on RXR (r = -.440, p = .001; Bonferroni Corrected p = .014). Other scales were not significantly related to functional connectivity, including *SOM*, *MAN*, *ANT*, *ALC*, *DRG*, *AGG*, *NON*, *DOM*, and *WRM* (all $rs \leq .24$, all *p-values* > .07). Together, these findings suggest that when the vmPFC and amygdala covaried together positively, participants had higher psychopathology scores on several hypothesized scales, but as these regions showed greater negative connectivity, the severity of psychopathology scores was lower. Figure 7 shows that removing the effects of insomnia complaints had only minimal effects on the correlations between vmPFC-amygdala connectivity and PAI scores.

INSERT FIGURE 7 ABOUT HERE

Discussion

Consistent with predictions from prior work [14, 15], greater self-reported sleep the night before the assessment was significantly related to higher *Trait* EI scores and lower scores on several indices of psychopathology. Sleep duration the night before the scan was also negatively correlated with functional connectivity between the right vmPFC and amygdala. Moreover, the strength of this negative prefrontal-amygdala connectivity pattern was directly related to scores on *Trait* EI and psychopathology scales. Generally, the more strongly negative the functional connectivity, the higher the EI scores and less severe the psychopathology scores.

The present finding that greater self-reported nocturnal sleep duration was associated with higher *Trait* EI scores is in line with our previous work showing that total sleep deprivation was correlated with a decline on the same indices [14] and other evidence suggesting a link between fatigue and lower EI [33]. In our prior study, sleep deprivation led to degradation of several aspects of EI, including emotional self-awareness, perceived effectiveness in dealing with interpersonal relationship issues, and the ability to cope with stress. We currently show that EI is associated with the duration of sleep during a single night, as those who obtained fewer hours of sleep the night before the assessment achieved lower Total EQ-i scores than those who obtained the most sleep. In fact, those participants obtaining 8 or more hours of sleep typically had Total EQ-i scores about 10 points (i.e., about two thirds of a standard deviation) higher than those obtaining 6.5 hours of sleep or less the preceding night. Moreover, all five EQ-i composite subscales also showed significant positive correlations with sleep duration from the previous night. In contrast, we found no association between sleep and *Ability* EI, as assessed by the MSCEIT.

The current finding that *Trait*, but not *Ability*, EI is related to sleep duration is enlightening, as these two models conceptualize the EI construct in very different ways [34]. Whereas *Trait* EI taps subjective emotional experience, global mood and optimism, self-confidence, self-awareness, and self-perceived interpersonal sensitivity [35], *Ability* EI involves the accuracy of emotional perception, the ability to use emotional information to facilitate performance, the quality of reasoning about emotional information, and the capacity to regulate or manage emotions [25]. Our findings suggest that, within the range of sleep duration obtained by most people on a typical night, getting more sleep appears

to be reliably associated with better self-perceived emotional functioning, interpersonal attunement, coping capacity, self-confidence, and self-awareness, but is not reliably related to performance based capacities, such as reasoning about emotional information and solving emotional problems. To the extent that these varied aspects of EI involve distinct neuroanatomical regions [30], it makes sense that sleep deprivation may have differential effects on such traits and capacities.

Greater sleep duration the night before the assessment was also associated with lower scores on several indices of psychopathology from the PAI. Specifically, increased sleep time was most strongly associated with reduced severity of complaints associated with anxiety, depression, paranoia, and schizophrenia. These findings are congruent with previous findings showing that total sleep deprivation was associated with increased symptoms of psychopathology [15]. Together, these studies suggest that lack of sleep, or even modest curtailment of sleep may be associated with a subtle non-clinical elevation of a number of emotional distress complaints, even among healthy normal individuals.

While reduced sleep has long been perceived as a consequence or symptom of psychopathology, emerging evidence suggests that sleep disruption may also play a contributory role in the etiology of some psychiatric conditions. A recent large-scale study showed that behaviorally induced insufficient sleep among adolescents was associated with a significantly elevated risk of suicidal ideation [36]. At present, the precise neurobiological basis for the link between sleep loss and psychopathology remains uncertain, but some evidence suggests that lack of sleep may lead to altered neurochemistry within the prefrontal cortex [37], alterations in neurotransmitter receptor sensitivity [38-40], and increases cortical excitability, particularly in prefrontal regions [41].

Considerable evidence points to dysfunction of the vmPFC during a number of psychopathological conditions including depression [42-45] anxiety disorders [46-49], and psychopathy [50]. Metabolic activity in the vmPFC also appears to be particularly affected by sleep deprivation [16], and a number of studies have shown that tasks sensitive to vmPFC functioning are particularly impaired by lack of sleep [10, 51-53]. Notably, functional connectivity between the emotion regulating regions of the medial prefrontal cortex and the emotionally responsive regions of the limbic system, such as the amygdala and other cortical regions appears to be altered by sleep deprivation [19, 54].

In the present study, the correlation between self-reported sleep duration and functional connectivity between the prefrontal cortex and amygdala was also investigated. With greater sleep the night before the scan, there was stronger negative functional connectivity between the vmPFC and amygdala in the right hemisphere. Emerging evidence suggests that the medial prefrontal regions are critical to normal top-down regulation of the amygdala and other limbic emotional engagement systems [55]. Interestingly, this cortico-limbic regulatory capacity can be depleted by overuse or fatigue [18]. One interpretation of our findings, therefore, is that greater nocturnal sleep may facilitate the daily replenishment of this top-down regulatory capacity, leading to more effective modulation of affective responses by the prefrontal cortex. Of course, the correlational nature of the findings precludes the ability to draw directional conclusions. The present findings are consistent with those of Yoo and colleagues who found that 35 hours of sleep deprivation was associated with increased amygdala responsiveness to negative emotional stimuli and reduced functional connectivity between the medial prefrontal cortex and amygdala [19], but further extend these findings to more common

levels of occasional sleep curtailment or the short sleep periods experienced periodically by most people. The right-lateralized nature of the finding was not hypothesized, but is interesting in light of other findings suggesting that sleep deprivation may have a greater impairing effect on cognitive processes mediated by the right compared to left hemisphere [56-58].

The final question we addressed was whether the sleep-related strength of functional connectivity between the vmPFC and amygdala might correlate directly with EI and psychopathology scores. The functional connectivity values between these two regions was extracted for each participant and used to predict scores on measures of EI and psychopathology. Higher *Trait* EI, *Stress Management*, and *Adaptability* scores were associated with a pattern of greater negative prefrontal-amygdala functional connectivity. In contrast, no association was observed for *Ability* EI, suggesting that this aspect of the vmPFC-amygdala emotion regulation system appears to be more related to affective response traits rather than behaviorally measured emotional problem solving abilities. Similarly, we found that the strength of vmPFC-amygdala functional connectivity was modestly but significantly positively correlated with half of the psychopathology scales on the PAI, most notably depression, but also anxiety, paranoia, treatment rejection, and marginally to suicidal ideation. Although correlational in nature, these findings are consistent with a number of studies that have shown that affective regulation is associated with a negative relationship between the medial prefrontal cortex and the amygdala [55, 59] and that some forms of affective psychopathology may involve alteration or disruption of this neurocircuitry [46, 60, 61].

Some limitations should be borne in mind when interpreting these findings. First, we used a self-report index of sleep, which is likely to suffer from some loss in precision and reliability, particularly when compared to objective methods such as ambulatory electroencephalographic or actigraphic monitoring. Future studies would benefit from employing objective measurements of sleep. Second, while the present sample is relatively large for a neuroimaging study, our participants were all thoroughly screened to exclude clinical levels of psychopathology. Consequently, the present findings cannot be validly generalized to more severe forms of psychopathology. Third, because the findings from this study are correlational, it is not possible to determine the causal direction of the observed relationships or whether the findings may be due to an unmeasured third variable. While insomnia complaints, response biases, and age did not seem to account for most of the findings, it is possible that other unexplored variables might have contributed. Furthermore, although we collected data regarding the amount of sleep obtained the preceding night and attempted to tightly control the time of scan administration, we did not specifically control for wakeup time on the day of the scan. Thus, it is possible that this could have added some uncontrolled variance to the data, potentially obscuring some important relationships. This is particularly important in light of the fact that we had no objective control for level of vigilance within the scanner, such as simultaneous electroencephalography (EEG). Thus, it is not possible to conclusively determine whether the observed differences in functional connectivity might have been due to fluctuations in vigilance occurring during the scan. Future studies would benefit from the use of simultaneous EEG in this regard. Finally, we only examined functional connectivity between two regions, the vmPFC and amygdala. Emotional experience and

regulation are extraordinarily complex processes and undoubtedly encompasses a much larger neurocircuitry than the limited set of regions examined here. Future work will need to expand upon this neurocircuitry to include other candidate nodes such as the insular cortex, striatum, brainstem nuclei, and other higher order associative regions.

Nonetheless, with appropriate consideration to the aforementioned limitations, we believe the present study advances our understanding of the association between recent sleep, prefrontal-amygdala connectivity, and emotional functioning. These data suggest that even small variations in sleep of only an hour or two may be significantly associated with significant differences in some aspects of perceived emotional intelligence and the severity of psychological distress. Conversely, getting a full night of sleep appears to go hand-in-hand with bolstered emotional strength and mental health.

Acknowledgments: Zachary Schwab, B.S., assisted in preprocessing of functional data and Melissa Weiner, B.S., assisted in the collection of behavioral data. This study was supported by a USAMRAA grant (W81XWH-09-1-0730).

References

1. Goel N, Rao H, Durmer JS, Dinges DF. Neurocognitive consequences of sleep deprivation. Semin. Neurol. 2009;29:320-39.

2. Lim J, Dinges DF. Sleep deprivation and vigilant attention. Ann. N. Y. Acad. Sci. 2008;1129:305-22.

3. Killgore WDS. Effects of sleep deprivation on cognition. Prog. Brain Res. 2010;185:105-29.

4. Vandekerckhove M, Cluydts R. The emotional brain and sleep: an intimate relationship. Sleep. Med. Rev. 2010;14:219-26.

5. Penetar D, McCann U, Thorne D, et al. Caffeine reversal of sleep deprivation effects on alertness and mood. Psychopharmacology (Berl.) 1993;112:359-65.

6. Tempesta D, Couyoumdjian A, Curcio G, et al. Lack of sleep affects the evaluation of emotional stimuli. Brain Res. Bull. 2010;82:104-8.

7. Franzen PL, Gianaros PJ, Marsland AL, et al. Cardiovascular reactivity to acute psychological stress following sleep deprivation. Psychosom. Med. 2011;73:679-82.

8. Minkel JD, Banks S, Htaik O, et al. Sleep deprivation and stressors: evidence for elevated negative affect in response to mild stressors when sleep deprived. Emotion 2012;12:1015-20.

9. Kahn-Greene ET, Lipizzi EL, Conrad AK, Kamimori GH, Killgore WDS. Sleep deprivation adversely affects interpersonal responses to frustration. Pers. Indiv. Differ. 2006;41:1433-43.

10. Killgore WDS, Balkin TJ, Wesensten NJ. Impaired decision-making following 49 hours of sleep deprivation. J. Sleep Res. 2006;15:7-13.

11. Killgore WDS, Killgore DB, Day LM, Li C, Kamimori GH, Balkin TJ. The effects of 53 hours of sleep deprivation on moral judgment. Sleep 2007;30:345-52.

12. Olsen OK, Pallesen S, Eid J. The impact of partial sleep deprivation on moral reasoning in military officers. Sleep 2010;33:1086-90.

13. Tempesta D, Couyoumdjian A, Moroni F, Marzano C, De Gennaro L, Ferrara M. The impact of one night of sleep deprivation on moral judgments. Soc. Neurosci. 2011.

14. Killgore WDS, Kahn-Greene ET, Lipizzi EL, Newman RA, Kamimori GH, Balkin TJ. Sleep deprivation reduces perceived emotional intelligence and constructive thinking skills. Sleep Med. 2007;9:517-26.

15. Kahn-Greene ET, Killgore DB, Kamimori GH, Balkin TJ, Killgore WDS. The effects of sleep deprivation on symptoms of psychopathology in healthy adults. Sleep Med. 2007;8:215-21.

16. Thomas M, Sing H, Belenky G, et al. Neural basis of alertness and cognitive performance impairments during sleepiness. I. Effects of 24 h of sleep deprivation on waking human regional brain activity. J. Sleep Res. 2000;9:335-52.

17. Sokol-Hessner P, Camerer CF, Phelps EA. Emotion regulation reduces loss aversion and decreases amygdala responses to losses. Soc. Cogn. Affect. Neurosci. 2012.

18. Wagner DD, Heatherton TF. Self-regulatory depletion increases emotional reactivity in the amygdala. Soc. Cogn. Affect. Neurosci. 2012.

19. Yoo SS, Gujar N, Hu P, Jolesz FA, Walker MP. The human emotional brain without sleep--a prefrontal amygdala disconnect. Curr. Biol. 2007;17:R877-8.

20. Gujar N, Yoo SS, Hu P, Walker MP. Sleep deprivation amplifies reactivity of brain reward networks, biasing the appraisal of positive emotional experiences. J. Neurosci. 2011;31:4466-74.

21. Killgore WD, Schwab ZJ, Weiner MR. Self-reported nocturnal sleep duration is associated with next-day resting state functional connectivity. Neuroreport 2012;23:741-5.

22. First MB, Spitzer RL, Gibbon M, Williams JBW. Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version, Patient Edition. (SCID-I/P). New York: Biometrics Research Department, New York State Psychiatric Institute, 2002.

23. Horne JA, Ostberg O. A self-assessment questionnaire to determine morningness-eveningness in human circadian rhythms. Int. J. Chronobiol. 1976;4:97-110.

24. Bar-On R. BarOn Emotional Quotient Inventory: A measure of emotional intelligence--Technical Manual. North Tonawanda, NY: Multi-Health Systems, 2002.

25. Mayer JD, Salovey P, Caruso DR. Mayer-Salovey-Caruso Emotional Intelligence Test (MSCEIT) User's Manual. North Tonawanda, NY: MHS, 2002.

26. Morey LC. Personality Assessment Inventory. Lutz, FL: Psychological Assessment Resources, Inc., 1991.

27. Whitfield-Gabrieli S, Nieto-Castanon A. Conn: a functional connectivity toolbox for correlated and anticorrelated brain networks. Brain Connect 2012;2:125-41.

28. Behzadi Y, Restom K, Liau J, Liu TT. A component based noise correction method (CompCor) for BOLD and perfusion based fMRI. Neuroimage 2007;37:90-101.

29. Tzourio-Mazoyer N, Landeau B, Papathanassiou D, et al. Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. Neuroimage 2002;15:273-89.

30. Killgore WD, Weber M, Schwab ZJ, et al. Gray matter correlates of Trait and Ability models of emotional intelligence. Neuroreport 2012;23:551-5.

31. Joo EY, Tae WS, Kim ST, Hong SB. Gray Matter Concentration Abnormality in Brains of Narcolepsy Patients. Korean J. Radiol. 2009;10:552-8.

32. Killgore WDS, Schwab ZJ, Kipman M, DelDonno SR, Weber M. Voxel-based morphometric gray matter correlates of daytime sleepiness. Neurosci. Lett. 2012;518:10-3.

33. Brown RF, Schutte NS. Direct and indirect relationships between emotional intelligence and subjective fatigue in university students. J. Psychosom. Res. 2006;60:585-93.

34. Brackett MA, Mayer JD. Convergent, discriminant, and incremental validity of competing measures of emotional intelligence. Pers. Soc. Psychol. Bull. 2003;29:1147-58.

35. Bar-On R. The Bar-On model of emotional-social intelligence (ESI). Psicothema 2006;18 Suppl:13-25.

36. Lee YJ, Cho SJ, Cho IH, Kim SJ. Insufficient sleep and suicidality in adolescents. Sleep 2012;35:455-60.

37. Bernier D, Bartha R, Devarajan S, Macmaster FP, Schmidt MH, Rusak B. Effects of overnight sleep restriction on brain chemistry and mood in women with unipolar depression and healthy controls. J. Psychiatry Neurosci. 2009;34:352-60.

38. Novati A, Roman V, Cetin T, et al. Chronically restricted sleep leads to depression-like changes in neurotransmitter receptor sensitivity and neuroendocrine stress reactivity in rats. Sleep 2008;31:1579-85.

39. Roman V, Walstra I, Luiten PG, Meerlo P. Too little sleep gradually desensitizes the serotonin 1A receptor system. Sleep 2005;28:1505-10.

40. Roman V, Hagewoud R, Luiten PG, Meerlo P. Differential effects of chronic partial sleep deprivation and stress on serotonin-1A and muscarinic acetylcholine receptor sensitivity. J. Sleep Res. 2006;15:386-94.

41. Huber R, Maki H, Rosanova M, et al. Human cortical excitability increases with time awake. Cereb. Cortex 2013;23:1-7.

42. Mayberg HS. Limbic-cortical dysregulation: a proposed model of depression. J. Neuropsychiatry Clin. Neurosci. 1997;9:471-81.

43. Drevets WC, Price JL, Simpson JR, Jr., et al. Subgenual prefrontal cortex abnormalities in mood disorders. Nature 1997;386:824-7.

44. Drevets WC, Ongur D, Price JL. Reduced glucose metabolism in the subgenual prefrontal cortex in unipolar depression. Mol. Psychiatry 1998;3:190-1.

45. Drevets WC. Prefrontal cortical-amygdalar metabolism in major depression. Ann. N. Y. Acad. Sci. 1999;877:614-37.

46. Etkin A, Wager TD. Functional neuroimaging of anxiety: a meta-analysis of emotional processing in PTSD, social anxiety disorder, and specific phobia. Am. J. Psychiatry 2007;164:1476-88.

47. Etkin A, Egner T, Kalisch R. Emotional processing in anterior cingulate and medial prefrontal cortex. Trends Cogn Sci 2011;15:85-93.

48. Rauch SL, Shin LM, Phelps EA. Neurocircuitry models of posttraumatic stress disorder and extinction: human neuroimaging research--past, present, and future. Biol. Psychiatry 2006;60:376-82.

49. Shin LM, Liberzon I. The neurocircuitry of fear, stress, and anxiety disorders. Neuropsychopharmacology 2010;35:169-91.

50. Blair RJ. The amygdala and ventromedial prefrontal cortex: functional contributions and dysfunction in psychopathy. Philos. Trans. R. Soc. Lond. B. Biol. Sci. 2008;363:2557-65.

51. Chuah LY, Dolcos F, Chen AK, Zheng H, Parimal S, Chee MW. Sleep deprivation and interference by emotional distracters. Sleep 2010;33:1305-13.

52. Libedinsky C, Smith DV, Teng CS, et al. Sleep deprivation alters valuation signals in the ventromedial prefrontal cortex. Front. Behav. Neurosci. 2011;5:70.

53. Venkatraman V, Huettel SA, Chuah LY, Payne JW, Chee MW. Sleep deprivation biases the neural mechanisms underlying economic preferences. J. Neurosci. 2011;31:3712-8.

54. De Havas JA, Parimal S, Soon CS, Chee MW. Sleep deprivation reduces default mode network connectivity and anti-correlation during rest and task performance. Neuroimage 2012;59:1745-51.

55. Quirk GJ, Likhtik E, Pelletier JG, Pare D. Stimulation of medial prefrontal cortex decreases the responsiveness of central amygdala output neurons. J. Neurosci. 2003;23:8800-7.

56. Cote KA, Milner CE, Osip SL, Baker ML, Cuthbert BP. Physiological arousal and attention during a week of continuous sleep restriction. Physiol. Behav. 2008;95:353-64.

57. Manly T, Dobler VB, Dodds CM, George MA. Rightward shift in spatial awareness with declining alertness. Neuropsychologia 2005;43:1721-8.

58. Pallesen S, Johnsen BH, Hansen A, et al. Sleep deprivation and hemispheric asymmetry for facial recognition reaction time and accuracy. Percept. Mot. Skills 2004;98:1305-14.

59. Ochsner KN, Ray RD, Cooper JC, et al. For better or for worse: neural systems supporting the cognitive down- and up-regulation of negative emotion. Neuroimage 2004;23:483-99.

60. Killgore WDS, Yurgelun-Todd DA. Ventromedial prefrontal activity correlates with depressed mood in adolescent children. Neuroreport 2006;17:167-71.

61. Koenigs M, Grafman J. Posttraumatic stress disorder: the role of medial prefrontal cortex and amygdala. Neuroscientist 2009;15:540-8.

Table 1. Means and Intercorrelations among Sleep Variables

Variable	Mean (SD)	1.	2.	3.	4.	5.	6.	7.	8.
1. Age (yrs)	30.15 (8.01)	--	.38*	-.02	-.27*	-.36*	-.37*	-.63**	-.02
2. MEQ	49.90 (10.27)		--	.23	-.34*	-.38*	-.50**	-.62**	.18
3. Sleep Last Night (h)	6.97 (1.07)			--	.04	-.03	.00	-.09	.72**
4. Weeknight Bedtime (h)	23:04 (03:13)				--	.96**	.74**	.63**	-.13
5. Weekend Bedtime (h)	23:56 (03:23)					--	.58**	.79**	-.15
6. Weekday Wakeup (h)	07:23 (01:37)						--	.72**	-.16
7. Weekend Wakeup (h)	08:38 (01:57)							--	-.15
8. Sleep Debt (h)	-00:26 (01:03)								--

MEQ = Morningness-Eveningness Questionnaire; Sleep Debt = Sleep Last Night - (((Average Weekday Sleep *5) + (Average Weekend Sleep *2))/7); *p < .05, **p < .001

Table 2. Connectivity Values Between the vmPFC and Amygdala

	Left Amygdala	Right Amygdala
Seed Region	*M* (*SD*) Range	*M* (*SD*) Range
Left vmPFC	.13 (.14) -.13 to .51	.13 (.13) -.19 to .42
Right vmPFC	.13 (.14) -.21 to .57	.14 (.13) -.13 to .47

Values reflect Fisher transformed correlation coefficients (i.e., z-scores). vmPFC = ventromedial prefrontal cortex (i.e., gyrus rectus).

Figure Legends

Figure 1. Mean emotional intelligence scores for the entire sample ($n = 65$) divided by terciles for Sleep Last Night, including Low Sleep (≤ 6.5 hours, $n = 22$), Moderate Sleep (6.6 – 7.9 hours, $n = 21$), and High Sleep (≥ 8 hours, $n = 22$). A) Analysis of variance indicated a significant main effect of sleep on scores on the Bar-On EQ-i ($p = .032$), with a significant difference between the High and Low Sleep groups. B) There was no main effect of sleep on the Mayer-Salovey-Caruso Emotional Intelligence Test (MSCEIT). *$p < .05$, corrected.

Figure 2. Effect sizes of the correlations between hours of self-reported sleep obtained the preceding night and scores on the Bar-On Emotional Intelligence Inventory (EQ-i) and the Mayer-Salovey-Caruso Emotional Intelligence Test (MSCEIT). Black bars: All scales of the EQ-i showed significant Pearson correlations with *Sleep Last Night*, whereas none of the MSCEIT scales showed significant correlations. Gray bars: Similar trends were observed after statistically controlling for insomnia complaints, but only Adaptability remained significant. *$p < .05$, **$p < .005$.

Figure 3. Effect sizes of the correlations between hours of self-reported sleep obtained the preceding night and scores on the Personality Assessment Inventory (PAI). Black bars: Greater sleep the preceding night was associated with lower scores on several indices of psychopathology based on bivariate correlations. Gray Bars: Most of the

correlations between *Sleep Last Night* and psychopathology remained significant after statistically controlling for insomnia complaints. *$p < .05$, **$p < .005$.

Figure 4. Functional connectivity maps for the left and right vmPFC seed regions of interest (ROIs). The brain images show axial slices that include both the vmPFC and amygdala regions. The white arrows show the location of the amygdala target ROIs. The maps were set to a whole brain threshold of $p < .05$, FWE corrected for multiple comparisons.

Figure 5. Self-reported *Sleep Last Night* was significantly correlated with negative functional connectivity between the right ventromedial prefrontal cortex (vmPFC) and the right amygdala. The figure shows the cluster in the right amygdala [MNI coordinates: x = 24, y = 2, z = -22] that showed negative functional connectivity with the right vmPFC seed region as a function of greater reported sleep time. For visualization, the cluster is height thresholded at ($p < .001$, uncorrected, spatial extent $p < .05$ FWE-corrected). Figures are displayed in sagittal (top left), axial (bottom left), and coronal (top right) views. The scatterplot (bottom right) shows the linear relationship between hours of sleep and the connectivity values extracted from the displayed cluster.

Figure 6. Effect sizes show the correlations between the magnitude of ventromedial prefrontal cortex (vmPFC) – amygdala functional connectivity and scores on the Bar-On Emotional Intelligence Inventory (EQ-i) and the Mayer-Salovey-Caruso Emotional Intelligence Test (MSCEIT). Black bars: Total EQ-i, as well as composite scale scores

for Stress Management and Adaptability showed significant negative bivariate correlations with functional connectivity, indicating that higher emotional intelligence on the EQ-i was associated with greater *negative connectivity* between these two regions. In contrast, MSCEIT scales were not significantly correlated with functional connectivity between these two regions. Gray bars: After controlling for insomnia complaints, the observed correlations with emotional intelligence were no longer significant. *$p < .05$.

Figure 7. Effect sizes show the correlations between the magnitude of ventromedial prefrontal cortex (vmPFC) – amygdala functional connectivity and scores on the Personality Assessment Inventory (PAI). Black Bars: Scores on several PAI scales showed positive bivariate correlations with functional connectivity, indicating that symptoms of psychopathology tended to be higher as these two regions covaried positively together, while psychopathology was reduced as these two regions covaried negatively with one another. Gray bars: Partial correlations controlling for insomnia complaints remained significant for the majority of PAI scales. *$p < .05$, **$p < .005$.

Figure 1

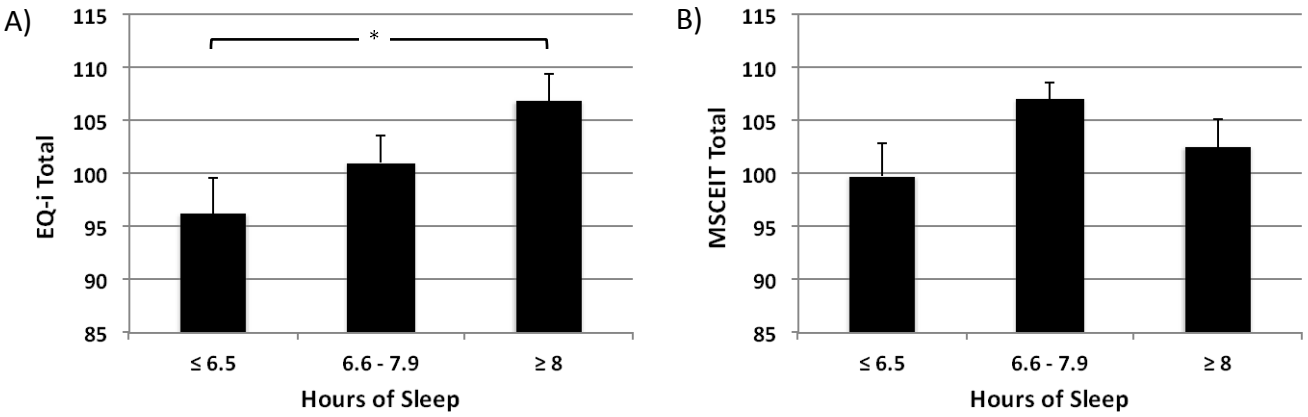

A)
115
110
105
100
95
90
85
EQ-i Total
*
≤ 6.5
6.6 - 7.9
≥ 8
Hours of Sleep
B)
115
110
105
100
95
90
85
MSCEIT Total
≤ 6.5
6.6 - 7.9
≥ 8
Hours of Sleep

Figure 2

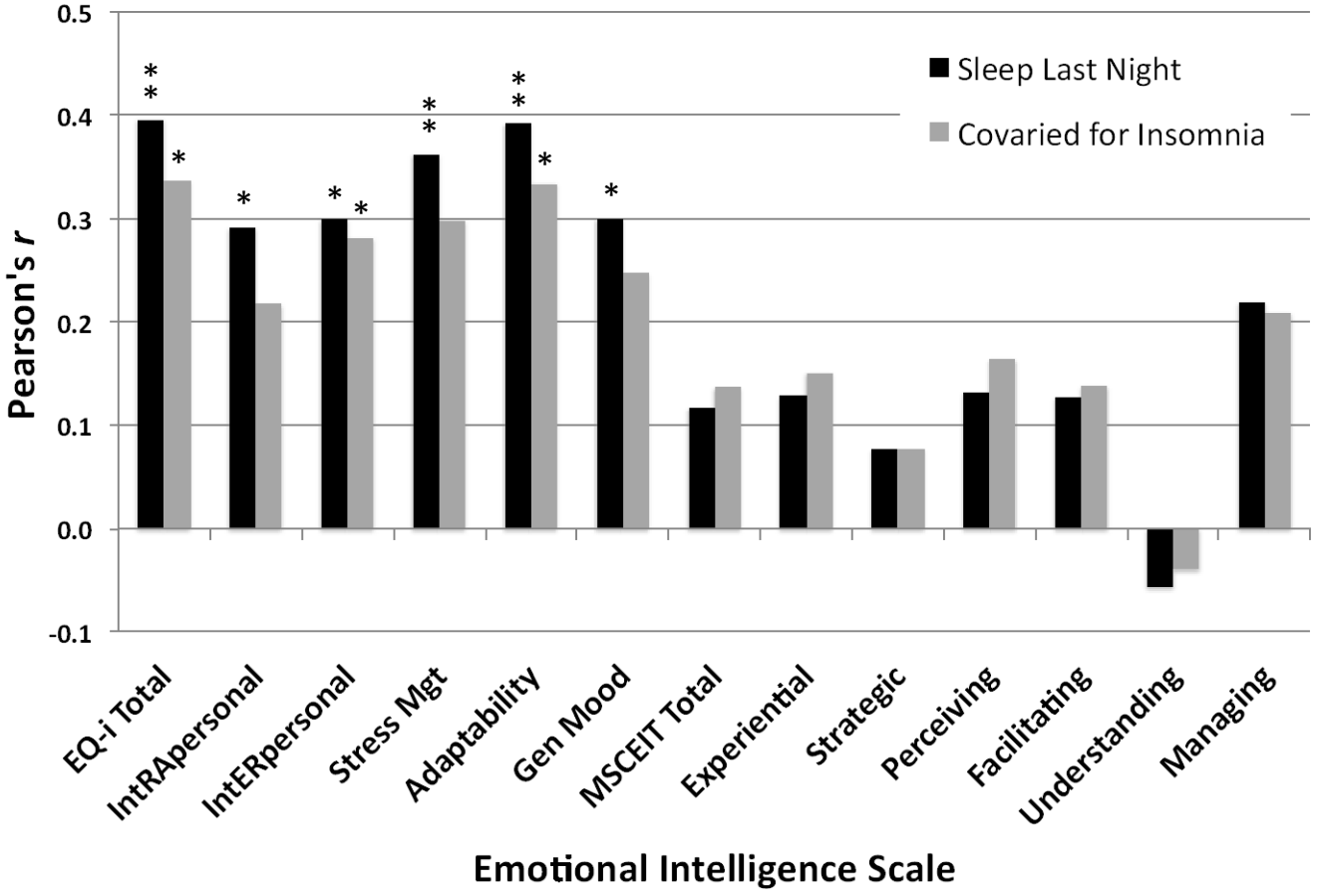

0.5
0.4
0.3
0.2
0.1
0.0
-0.1
Pearson's r
Sleep Last Night
Covaried for Insomnia
EQ-i Total
IntRApersonal
IntERpersonal
Stress Mgt
Adaptability
Gen Mood
MSCEIT Total
Experiential
Strategic
Perceiving
Facilitating
Understanding
Managing
Emotional Intelligence Scale

Figure 3

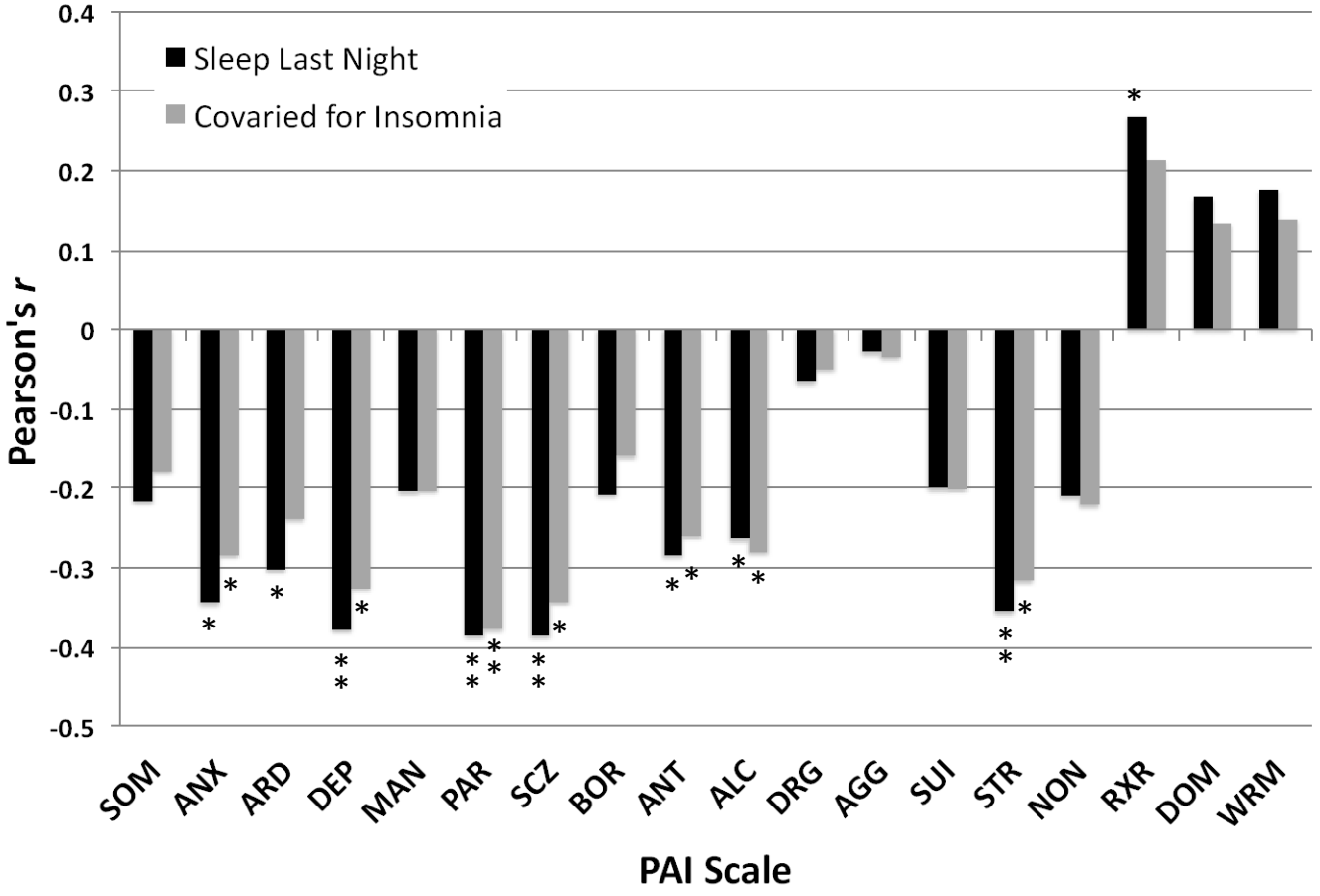

Sleep Last Night
Covaried for Insomnia
Pearson's r
0.4
0.3
0.2
0.1
0
-0.1
-0.2
-0.3
-0.4
-0.5
SOM
ANX
ARD
DEP
MAN
PAR
SCZ
BOR
ANT
ALC
DRG
AGG
SUI
STR
NON
RXR
DOM
WRM
PAI Scale

Figure 4

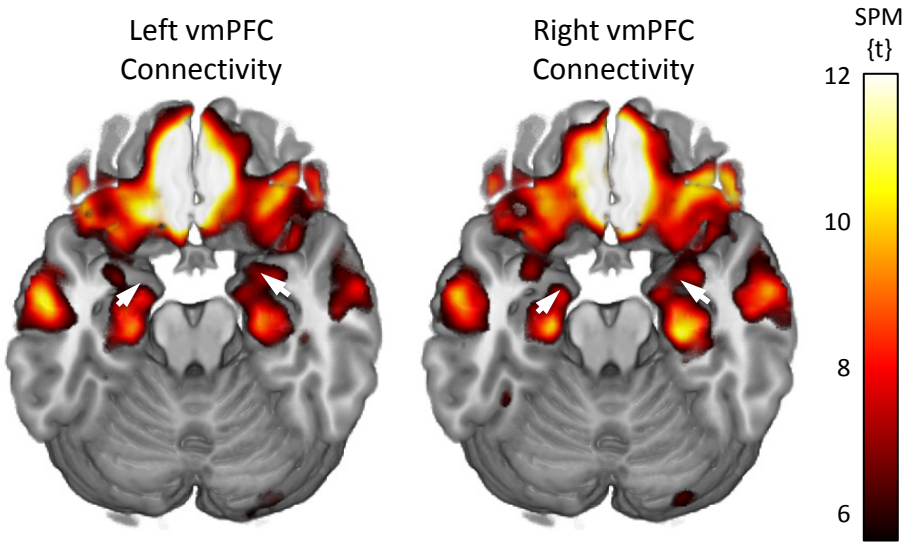

Left vmPFC
Connectivity
Right vmPFC
Connectivity
SPM
{t}
12
10
8
6

Figure 5

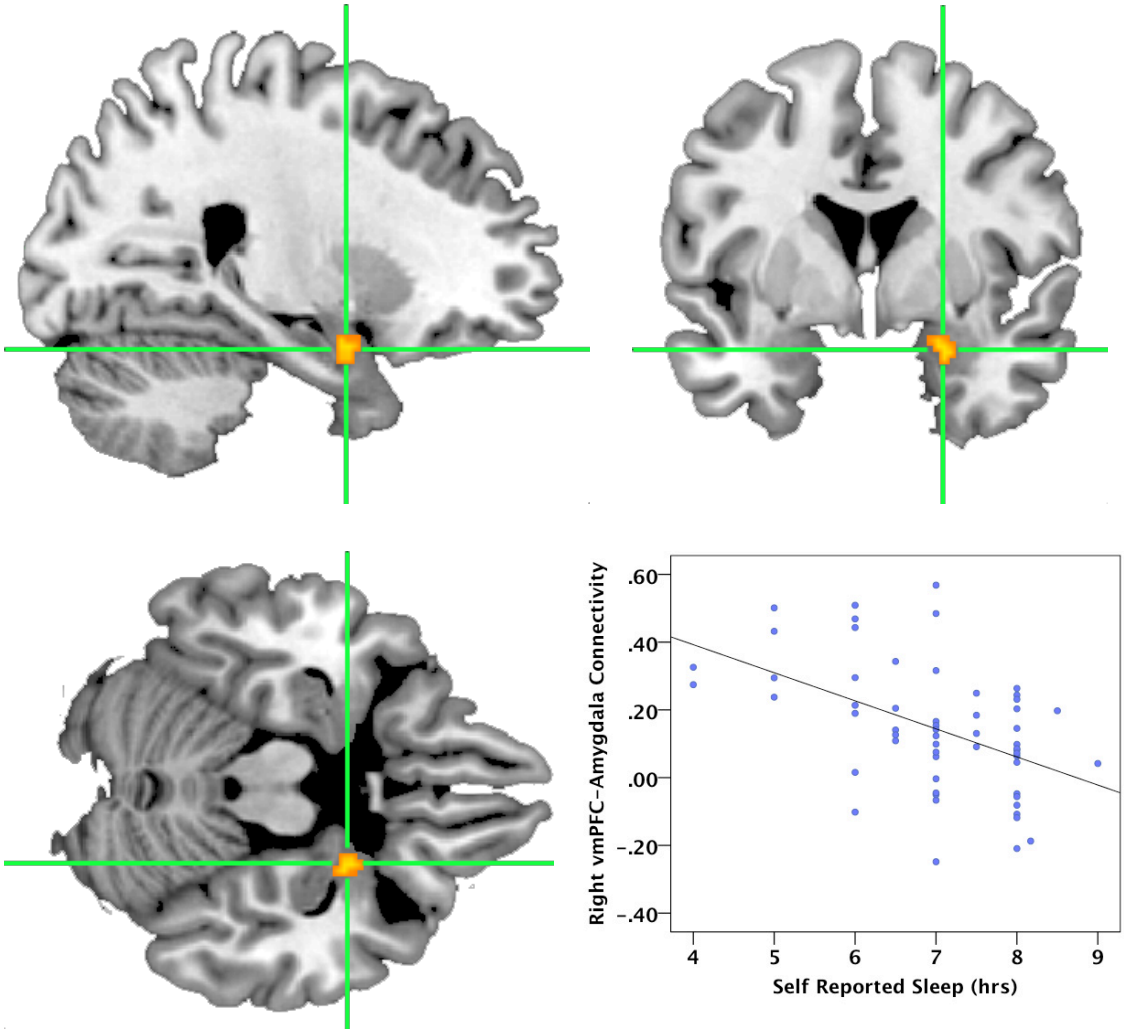

Right vmPFC–Amygdala Connectivity
.60
.40
.20
.00
-.20
-.40
4
5
6
7
8
9
Self Reported Sleep (hrs)

Figure 6

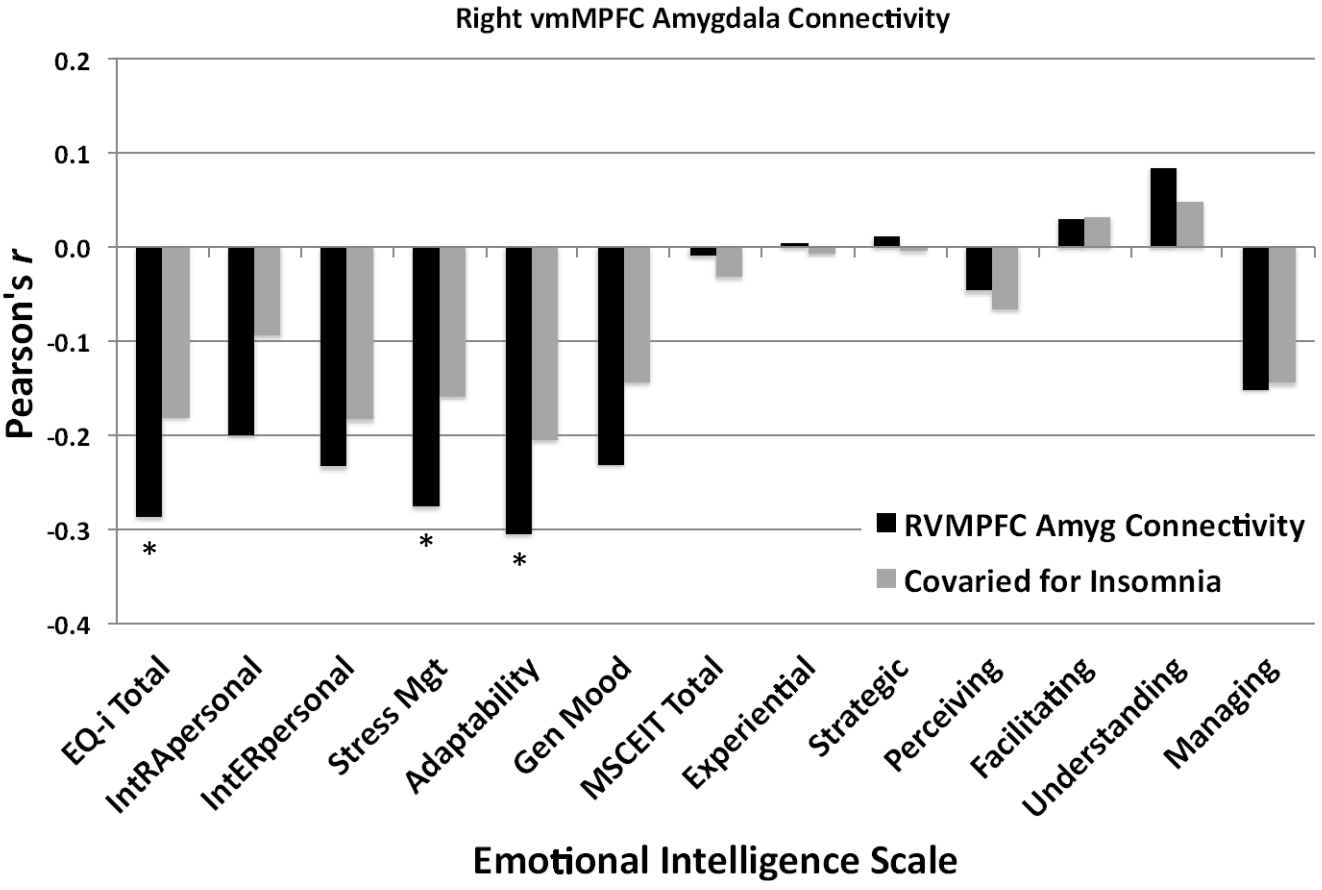
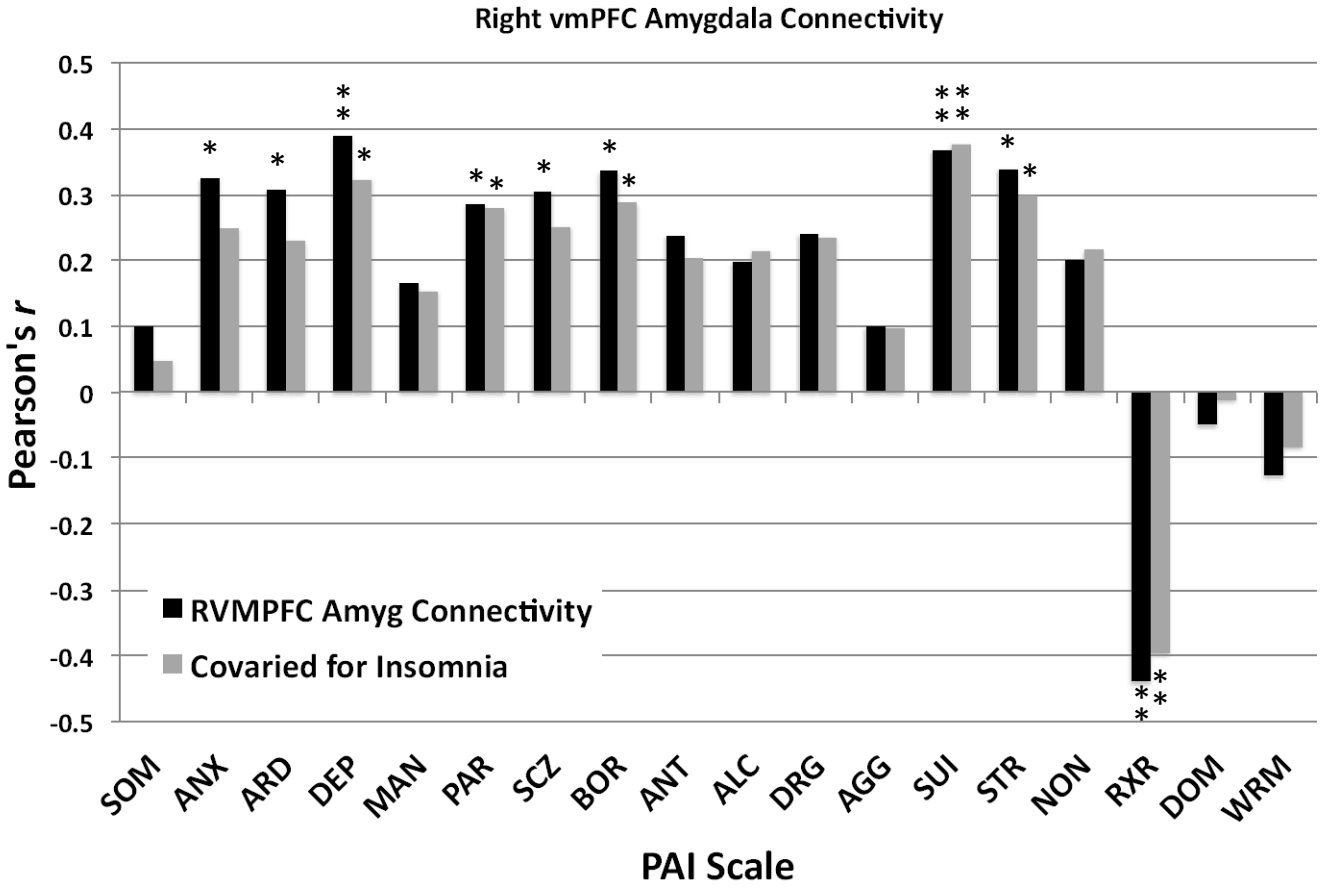

Right vmMPFC Amygdala Connectivity
0.2
0.1
0.0
-0.1
-0.2
-0.3
-0.4
Pearson's r
*
*
*
RVMPFC Amyg Connectivity
Covaried for Insomnia
EQ-i Total
IntRApersonal
IntERpersonal
Stress Mgt
Adaptability
Gen Mood
MSCEIT Total
Experiential
Strategic
Perceiving
Facilitating
Understanding
Managing
Emotional Intelligence Scale

Figure 7


Right vmPFC Amygdala Connectivity
Pearson's r
0.5
0.4
0.3
0.2
0.1
0
-0.1
-0.2
-0.3
-0.4
-0.5
RVMPFC Amyg Connectivity
Covaried for Insomnia
SOM
ANX
ARD
DEP
MAN
PAR
SCZ
BOR
ANT
ALC
DRG
AGG
SUI
STR
NON
RXR
DOM
WRM
PAI Scale

SOCIAL NEUROSCIENCE, 2013
Vol. 8, No. 4, 334–346, http://dx.doi.org/10.1080/17470919.2013.807300

Emotional intelligence correlates with functional responses to dynamic changes in facial trustworthiness

William D. S. Killgore, Zachary J. Schwab, Olga Tkachenko, Christian A. Webb, Sophie R. DelDonno, Maia Kipman, Scott L. Rauch, and Mareen Weber

Social, Cognitive and Affective Neuroscience Lab, McLean Hospital, Harvard Medical School, Belmont, MA, USA

Emotional intelligence (EI) refers to a constellation of traits, competencies, or abilities that allow individuals to understand emotional information and successfully navigate and solve social/emotional problems. While little is known about the neurobiological substrates that underlie EI, some evidence suggests that these capacities may involve a core neurocircuitry involved in emotional decision-making that includes the ventromedial prefrontal cortex (vmPFC), anterior cingulate cortex (ACC), insula, and amygdala. In a sample of 39 healthy volunteers (22 men; 17 women), scores on the Bar-On EQ-i (a trait/mixed model of EI) and Mayer–Salovey–Caruso Emotional Intelligence Test (MSCEIT; an ability model of EI) were correlated with functional magnetic resonance imaging responses during brief presentations of moving facial expressions that changed in the level of perceived trustworthiness. Core emotion neurocircuitry was responsive to dynamic changes in facial features, regardless of whether they reflected increases or decreases in apparent trustworthiness. In response to facial movements indicating decreasing trustworthiness, MSCEIT correlated positively with functional responses of the vmPFC and rostral ACC, whereas the EQ-i was unrelated to regional activation. Systematic differences in EI ability appear to be significantly related to the responsiveness of the vmPFC and rostral ACC to facial movements suggesting potential trustworthiness.

Keywords: Emotional intelligence; Somatic Marker Hypothesis; Ventromedial prefrontal cortex; Amygdala; Insula.

Human beings vary widely in their ability to acquire new information, understand their environment, think rationally, apply their knowledge to adapt to changing conditions, solve problems, and achieve goals. Broadly speaking, these capacities comprise what is known as "intelligence" (Wechsler, 1958). While the concept of intelligence as a unitary construct has persisted for over a century, some authors have hypothesized the possible existence of multiple forms of intelligence (Gardner, 1983). In particular, the construct of emotional intelligence (EI) has garnered considerable interest both within scientific and popular writings since the mid-1990s (Bar-On, 2006; Goleman, 1995; Mayer, Salovey, Caruso, & Sitarenios, 2001). While scholars differ in the exact criteria used to define EI, most current conceptualizations generally agree that the construct involves some constellation of traits, competencies, or abilities that allow an individual to understand emotional information and successfully navigate and solve social/emotional problems (Bar-On, 2006; Mayer et al., 2001). From one perspective, EI is described as a relatively stable constellation of emotionally related competencies and traits that underlie the potential to cope adaptively with demanding situations and to use emotional knowledge to succeed in achieving goals (Bar-On, 2006). This *Trait* (or Mixed) model views EI as similar in many ways to personality, though more modifiable through life experience and reflection (Webb et al., 2013). In contrast, the *Ability* model of EI defines the construct

Correspondence should be addressed to: William D. S. Killgore, Ph.D., Social, Cognitive and Affective Neuroscience Lab, McLean Hospital, Harvard Medical School, 115 Mill Street, Belmont, MA 02478, USA. E-mail: killgore@mclean.harvard.edu

This research was supported by a USAMRAA grant (W81XWH-09-1-0730).

in terms of measurable performance on tasks requiring the ability to solve emotional problems as well as demonstrate reasoning and knowledge about emotional processes (Webb et al., 2013). Both theoretical models continue to be actively researched and both have yielded well-normed, standardized, commercially available tests (Brackett & Mayer, 2003). At present, however, there exists very little scientific understanding of the neurocircuitry involved in EI.

One hypothesized model of the neurocircuitry underlying EI was proposed by Bar-On and colleagues (Bar-On, Tranel, Denburg, & Bechara, 2003), and suggests that the key features of EI can be parsimoniously explained by the emotional decision-making circuitry outlined by Antonio Damasio (Damasio, 1996), known as the Somatic Marker Circuitry (SMC) (Bar-On et al., 2003; Bechara & Damasio, 2005). The Somatic Marker Hypothesis (SMH) essentially provides an explanation of how the brain learns from emotional experiences and uses "somatically remembered" experiential knowledge to influence future decisions (Damasio, 1994). Simply put, the SMH suggests that our cognitive deliberations during decision-making are aided by emotional body signals, "hunches," or "gut feelings" that were initially formed through prior experience with a stimulus or situation, and that are automatically reactivated during future encounters resembling the earlier experience. According to the SMH, three primary brain structures (in addition to many secondary ones) are involved in the development of these somatic biasing signals to influence judgment and decision-making. First, the amygdala is proposed to be responsible for triggering initial signals of emotional salience in response to a relevant stimulus that leads to enactment of the somatic states characteristic of an emotion. Second, the insula contributes to the "feeling" of emotion by neurally mapping these somatosensory and visceral sensations, which can later be "simulated" within the brain when a comparable emotion-evoking stimulus is encountered in the future. Finally, the ventromedial prefrontal cortex (vmPFC) is posited as the core integrative system that joins these somatic signals with past and present cognitive representations of stimuli and situations. Once a stimulus has been associated with a pleasant or unpleasant feeling (i.e., a somatic marker), future reactivation of these cognitive representations of the stimulus (or actual re-encounters) can evoke a similar somatic experience (i.e., a "good" or "bad" feeling), biasing subsequent judgments and decisions toward advantageous outcomes. Bar-On and colleagues suggest that the SMC is the primary neurocircuitry that underlies the capabilities and competencies that comprise EI (Bar-On et al., 2003). The anterior cingulate cortex, particularly in the rostral regions, may also serve as part of the extended medial prefrontal cortex as it plays a key role in regulating emotion and resolving emotional conflict (Etkin, Egner, & Kalisch, 2011; Etkin, Egner, Peraza, Kandel, & Hirsch, 2006).

Some data from neuroimaging studies now exist to support the role of the SMC in EI. Based on the assumption that EI capacities involve reasoning and problem solving about emotion, most studies of the neurobiological basis of this construct have focused on prefrontal cortical regions involved in problem solving and emotional regulation, as well as somatic and emotional processing regions such as the insular cortex and amygdala. Early studies using functional magnetic resonance imaging (fMRI) showed that activation of some of these hypothesized regions of the brain, particularly the medial prefrontal cortex, was negatively correlated with measures of *Ability* EI (Reis et al., 2007) and *Trait* EI (Killgore & Yurgelun-Todd, 2007). The inverse relationships between EI and brain responses to these very simple task designs, using static fearful facial expressions or rule-based card selection tasks, were interpreted as evidence of neural efficiency, suggesting that individuals possessing greater EI were able to engage in emotional processing with less neural and cognitive effort (Killgore & Yurgelun-Todd, 2007). Whereas those initial studies compared emotional/social-processing tasks to resting baseline, a subsequent study using a more complex auditory paradigm with a nonresting comparison condition found positive correlations between EI and some cortical emotional processing regions, while failing to find activation in more primitive regions such as the amygdala (Kreifelts, Ethofer, Huberle, Grodd, & Wildgruber, 2010). Recent structural neuroimaging studies have also suggested that measures of EI are related to gray matter volume within the vmPFC (Killgore et al., 2012; Koven, Roth, Garlinghouse, Flashman, & Saykin, 2011; Takeuchi et al., 2011), further supporting this region as a potentially important contributor to EI capacities.

A key aspect of social and emotional intelligence involves the ability to discriminate between individuals who are safe to approach and those who should be avoided (Winston, Strange, O'Doherty, & Dolan, 2002). The amygdala, one of the regions involved in the SMC, appears to be critical to this process. Prior work has shown that lesions to the amygdala can impair the ability to distinguish between trustworthy and untrustworthy individuals based on facial appearance (Adolphs, Tranel, & Damasio, 1998) and that such lesions often lead to inappropriate levels of social trust (Koscik & Tranel, 2011). Other work suggests that the vmPFC is also important to these types of

social judgments involving the ability to discriminate trustworthy from untrustworthy individuals (Koscik & Tranel, 2011). The vmPFC may be especially important in the process of integrating social, emotional, and cognitive information for determining trustworthiness decisions (Bzdok et al., 2012; Damasio, 1994). While the vmPFC is highly complex and involved in many aspects of social and emotional functioning, consistent evidence suggests that it is particularly activated when a person is considering the mental state or goals of another person (Frith, 2007). At present, no research has examined the relationship between EI capacities and the responsiveness of these brain regions to social trust stimuli.

The goal of the present study was to build upon the prior work evaluating the relationship between EI and SMC responses to simple static facial expressions by using a more ecologically valid task of processing dynamically changing facial attributes affecting trustworthiness judgments. In the "real world," facial features are rarely static, and clues to the intentions of others often come from the subtle changes in facial movement that occur during interpersonal exchanges. Here, during fMRI, we presented healthy participants with brief glimpses of faces that rapidly and dynamically changed in features associated with perceived trustworthiness. In each condition, faces either morphed from appearing highly trustworthy to neutral (i.e., decreasing in trustworthiness) or from low trustworthiness to neutral (i.e., increasing in trustworthiness). We hypothesized that higher scores on tests assessing both *Trait* and *Ability* models of EI would be associated with increased activation of the primary nodes of the SMC, particularly the vmPFC, in response to dynamically changing facial expressions indicative of decreasing trustworthiness.

METHODS

Participants

Thirty-nine right-handed healthy volunteers (22 men; 17 women) ranging in age from 18 to 45 years ($M = 29.9$, $SD = 8.6$) participated in the study. All participants had completed at least 11 years of formal education ($M = 15.0$, $SD = 2.0$) and were native English speakers. The sample was racially diverse, including 24 individuals self-identified as Caucasian (61.5%), 8 as African American (20.5%), 4 as Asian American (10.3%), and 3 as "other" or "multi-racial" (7.7%). Volunteers were recruited via Internet advertisements and posted flyers within the Boston metropolitan area and were paid for their participation. Based on a detailed screening interview including questions adapted from the Structured Clinical Interview for DSM-IV Disorders (SCID-I/P) (First, Spitzer, Gibbon, & Williams, 2002), potential subjects were excluded for any history of Axis I mental disorder, neurological illness, head injury with loss of consciousness >30 minutes, sleep-related disorder, current use of psychotropic medications or substances known to affect functional neuroimaging, or current chemotherapy or radiation therapy. Written informed consent was obtained from all participants. The McLean Hospital Institutional Review Board approved the procedures for this study.

Materials and procedure

Following completion of the informed consent process, each participant completed computerized administrations of two well-validated commercially available tests of EI. The Bar-On Emotional Quotient Inventory (EQ-i) (Bar-On, 2002) was included as an index of *Trait* (or Mixed) EI. The EQ-i comprises 125 self-report items that yield a *Total EQ* score and five composite scores (i.e., *Interpersonal*, *Intrapersonal*, *Adaptability*, *Stress Management*, and *General Mood*). Individuals scoring high on the *Interpersonal* scale describe themselves as empathic and interpersonally aware, while those scoring high on the *Intrapersonal* scale describe themselves as self-aware, in-tune with their own emotions, and high in self-esteem. High scorers on the *Adaptability* scale perceive themselves as objective problem solvers who can adapt quickly to new situations. Those high in *Stress Management* describe themselves as well-controlled and unflappable in difficult or stressful situations. Individuals with high scores on the *General Mood* scale are self-described positive thinkers who are content with life. All EQ-i scores were scaled based on the general normative group, without adjustment for sex. To measure *Ability* EI, participants also completed the Mayer–Salovey–Caruso Emotional Intelligence Test (MSCEIT) (Mayer, Salovey, & Caruso, 2002), which includes 141 computer-administered items to assess individual skill at identifying, understanding, and using emotions. The test presents the participants with various types of stimuli that have to be rated for emotional characteristics or potential solutions that need to be selected to effectively address a given emotionally salient situation. The MSCEIT yields a *Total EI* score and two area scores, *Experiential* EI and *Strategic* EI. High scorers on *Experiential* EI are skilled at perceiving emotions and are effective at using that information to facilitate thought and

performance. This area includes two subscales measuring abilities described as *Perceiving* and *Facilitating* emotions. The second area is *Strategic* EI. Those scoring high on this area have excellent capacity for understanding emotional information and are skilled at managing emotions in themselves and in others. *Strategic* EI comprises two subscales measuring abilities described as *Understanding* and *Managing* of emotions. MSCEIT scoring was based on the consensus scoring methods outlined in the manual (Mayer et al., 2002). Following completion of the EI tests, participants underwent structural and functional neuroimaging.

Dynamic facial trustworthiness task (DFTT)

During fMRI, participants completed a 4-minute task involving the visual perception of dynamically changing facial displays of trustworthiness. The face stimuli were selected from a freely available database (http://webscript.princeton.edu/~tlab/databases/database-6-trustworthiness-dataset/) of 100 computer-generated facial identities at three different trustworthiness levels. These faces were generated using the FaceGen 3.1 modeling program (http://facegen.com) and morphed to vary along the dimension of trustworthiness according to the methods described by Oosterhof and Todorov (2008). Briefly, that group used the computer-modeling program to generate 300 neutral faces of European origin, which were then subsequently rated by 29 judges on a 9-point scale of trustworthiness. By mathematically identifying the features in the faces that related to the dimension of trustworthiness, Oosterhof and Todorov (2008) randomly generated a new set of computer-generated faces varying systematically in these characteristics along a scale of standard deviation (SD) units. The stimuli used in the present study were pseudo-randomly drawn from a pool of 300 faces constructed from 100 distinct facial identities that varied along the dimension of trustworthiness at three different levels. All 100 facial identities were used, though only a subset was pseudo-randomly selected from each trustworthiness condition: 40 low trustworthy faces were selected from the 100 faces in the −3 SD data set; 60 neutral faces were selected from the 100 faces in the 0 SD data set; 40 high trustworthy faces were selected from the 100 faces in the 3 SD data set (see Figure 1).

During the DFTT, participants viewed brief presentations of faces that appeared to change expression. The DFTT comprised three different trial types: (1) *Decreasing Trustworthiness* (D; high trustworthy changing to neutral), (2) *Increasing Trustworthiness* (I; low trustworthy changing to neutral), and (3) *Neutral* (N; face identity change but no change in neutral trustworthiness level). Each trial was presented for 100 ms, with the first face (F1) shown for two screen refresh cycles (i.e., 33 ms), followed by the second face (F2) for four screen refresh cycles (i.e., 67 ms), and a 1400 ms intertrial interval (ITI). Thus, a new stimulus appeared every 1500 ms. This is essentially the same presentation speed as traditional digital video recording and gives the appearance of human-like movement on the face. During stimulus presentation, face identity change was not explicitly apparent, but the facial features appeared to subtly change expression.

Each of the F1 identities was always paired with a different identity at F2 in a pseudorandom fashion. All 100 face identities were used at F1 and 40 identities were recycled through to create a total of 140 trials, with the requirement that no F1 identity was ever

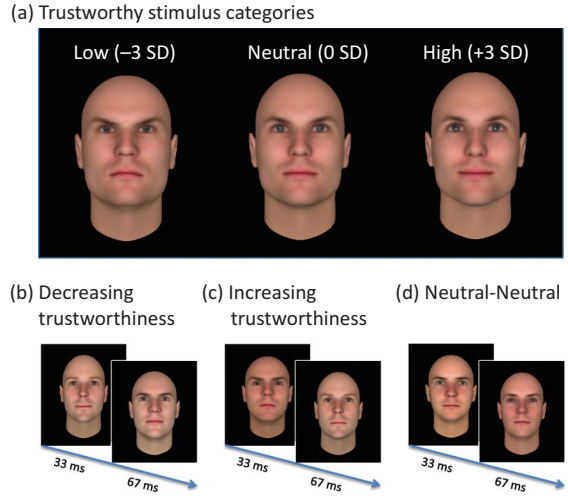


Figure 1. Examples of the stimuli used in the dynamic facial trustworthiness task (DFTT). Facial features were morphed along a continuum of trustworthiness according to the methods outlined by Oosterhof and Todorov (2008). (a) Three categories of faces were used, selected from those rated 3 SD below the mean in trustworthiness (left), those at the mean of trustworthiness (center), and those rated 3 SD above the mean in trustworthiness features (right). During the DFTT, pairs of faces were presented to give the appearance of subtle facial movement. (b) During the *Decreasing Trustworthiness* presentations, a high trustworthy face (+3 SD) was presented for 33 ms, followed by a neutral trustworthy face (0 SD) for 67 ms, which gave the impression of movement toward lesser trustworthiness. (c) During the *Increasing Trustworthiness* presentations, a low trustworthy face (–3 SD) was presented for 33 ms, followed by a neutral trustworthy face (0 SD) for 67 ms, which gave the impression of movement toward greater trustworthiness. (d) During the *Neutral* presentations, a neutral trustworthy face (0 SD) was presented for 33 ms, followed by a different neutral trustworthy face (0 SD) for 67 ms, which provided a control for potential movement effects associated with changing face identities independent of changes in trustworthiness.

shown twice for the same condition (e.g., if an identity was shown as a neutral expression at F1, it would either be shown again later as a high or low trustworthy face), and never appeared in two trials in a row. Notably, because the F2 faces were always neutral, both of the primary conditions reflect change from extremes in trustworthiness (high or low) toward the neutral intermediate appearance.

During the fMRI scan, the DFTT was presented in alternating 30-second blocks of the primary conditions flanked by 15 seconds of a crosshair fixation point (+) at either end of the task. The total duration of the task was 240 seconds with the following block order: +, N, D, I, N, I, D, N, +. Each of the seven 30-second blocks presented 20 trials (out of 140 trials total). To ensure that participants remained engaged with the task, they were required to make a simple button response with their dominant hand as quickly as possible each time the stimulus appeared on the screen.

Neuroimaging parameters

Participants underwent neuroimaging on a Tim Trio 3T scanner (Siemens, Erlangen, Germany) using a 12-channel head coil. Structural images were first acquired using a T1-weighted 3D MPRAGE sequence (TR/TE/flip angle = 2.1 s/2.25 ms/12°) over 128 sagittal slices (256 × 256 matrix) and a slice thickness of 1.33 mm (voxel size = 1 × 1 × 1.33 mm). T2*-weighted functional MRI scans were collected over 43 transverse slices (3.5 mm thickness, 0 skip) using an interleaved sequence (TR/TE/flip angle = 3.0 s/30 ms/90°), with 80 images collected per slice. Data were collected with a 22.4 cm field of view and a 64 × 64 acquisition matrix.

Image processing

The data were preprocessed and analyzed in SPM8 (http://www.fil.ion.ucl.ac.uk/spm/). According to standard algorithms, raw images were realigned to the first image in the series, unwarped, coregistered to each participant's high-resolution anatomical image, spatially normalized to the stereotaxic coordinate system of the Montreal Neurological Institute (MNI), spatially smoothed using an isotropic Gaussian kernel of 6 mm full-width at half-maximum (FWHM), and resliced to 2 × 2 × 2 mm voxels. The time series data were convolved with the SPM8 canonical hemodynamic response function, the AR(1) option was used to correct for serial autocorrelation, and low-frequency confounds were removed with the standard 128-second high-pass filter. Individual scans were visually inspected using the Artifact Detection Tool (http://www.nitrc.org/projects/artifact_detect/). Scan volumes exceeding 3 SD in mean global intensity or scan-to-scan motion that exceeded 1.0 mm were regressed out of the first-level analysis as a nuisance covariate.

Statistical analysis

For each participant, a general linear model was created to identify the regions showing greater task-related activation to the three primary task conditions, including the *Decreasing Trustworthiness, Neutral Trustworthiness,* and *Increasing Trustworthiness* blocks compared to the implicit baseline. Next, contrasts were created by comparing the *Decreasing Trustworthiness > Neutral*, *Increasing Trustworthiness > Neutral*, and *Decreasing Trustworthiness > Increasing Trustworthiness* conditions. The contrast images created from this analysis for each participant were carried forward as the dependent variables within second-level random effects regression analysis models with EI score as the predictor variable. Separate regression models were created for the EQ-i and MSCEIT predictors to examine the association between emotional intelligence and brain responses to changing levels of trustworthiness. Finally, based on the lack of amygdala findings for some of the *a priori* analyses, we undertook a series of additional *post-hoc* quadratic trend analyses to explore the possibility that some key regions might respond to trustworthiness in a curvilinear manner. Based on our *a priori* hypotheses, bilateral search territories including the primary emotional regulation and emotional response nodes of the SMC were created using the Wake Forest University PickAtlas Utility (Maldjian, Laurienti, Kraft, & Burdette, 2003) and the boundaries defined by the Automated Anatomical Labeling Atlas (Tzourio-Mazoyer et al., 2002). We focused on the bilateral gyrus rectus, ACC, and amygdala and insula bilaterally. Analyses were subjected to small volume correction for multiple comparisons within each search territory at $p < .001$ (uncorrected), $p < .10$, false discovery rate (FDR) corrected, k (extent) ≥ 10 contiguous voxels.

RESULTS

Primary comparisons

As evident in Table 1 and Figure 2, the *Decreasing Trustworthiness > Neutral* comparison was associated with significant activation within several regions of

TABLE 1
Locations of maximally activated voxels during primary trustworthiness comparisons

Comparison region	Cluster size (voxels)	MNI coordinates X	y	z	SPM {t}
Decreasing trustworthiness > Neutral					
R insula	16	46	−4	−6	3.83
Gyrus rectus	13	0	38	−16	3.68
R amygdala	10	24	2	−14	3.62
R insula	17	36	−20	12	3.55
Increasing trustworthiness > Neutral					
L amygdala	14	−20	−2	−20	4.81
R insula	40	34	−10	16	4.10
Gyrus rectus	15	0	30	−16	3.94

Notes: All analyses significant at $p < .001$, uncorrected; $p < .10$ (FDR, small volume corrected). R, right; L, left.

the SMC, including the right posterior insula, right amygdala, and medial gyrus rectus. On the other hand, the contrast between *Increasing Trustworthiness > Neutral* was associated with increased activation of the right anterior insula, left amygdala, and medial gyrus rectus (see Table 1 and Figure 2). These findings suggest that changes in facial trustworthiness are associated with significant activation of regions of the hypothesized neurocircuitry. However, when the *Increasing Trustworthiness* and *Decreasing Trustworthiness* conditions were directly contrasted, there were no regions showing significant differences.

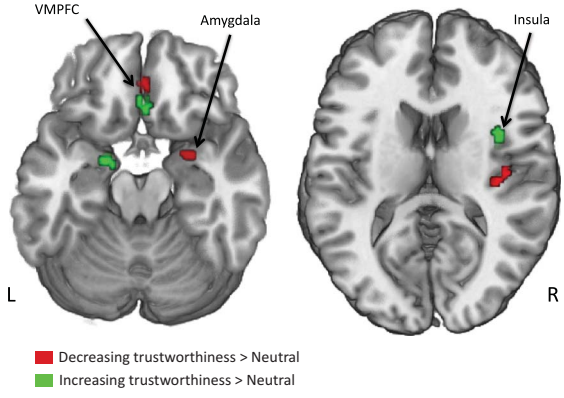


Figure 2. Regions of functional activation associated with the contrasts between *Decreasing Trustworthiness > Neutral* (red) and *Increasing Trustworthiness > Neutral* (green). Significance was evaluated using a small volume correction for multiple comparisons within each search territory at $p < .001$ (uncorrected), $p < .10$, FDR corrected, k (extent) ≥ 10. The image shows that the *Decreasing Trustworthiness > Neutral* contrast was associated with increased activation of the ventromedial prefrontal cortex (vmPFC) and right amygdala (left image), and posterior insula (right image). The *Increasing Trustworthiness > Neutral* contrast was also associated with increased activation of the vmPFC as well as the left amygdala (left image) and anterior insula (right image).

Bar-On EQ-i correlations

Within the hypothesized search regions, we found that Total EQ-i and subscale scores were not associated with functional activation in response to the *Decreasing Trustworthiness* or *Increasing Trustworthiness* conditions or the primary condition contrasts.

MSCEIT correlations

Total scores on the MSCEIT were not significantly correlated with activation during the *Increasing Trustworthiness* condition, but were positively correlated with a cluster of 22 activated voxels within the right vmPFC (i.e., gyrus rectus) [$x = 6$, $y = 32$, $z = -16$], $t(37) = 4.37$, $p = .09$ (FDR small volume corrected), during the *Decreasing Trustworthiness* condition (see Figure 3). Additionally, the beta parameters for each participant were extracted from the activated cluster region and correlated with the two area and four branch scores of the MSCEIT to identify the components of EI that contributed most to the observed effects. Only correlations below $p < .005$ are interpreted to avoid inflation of type I error. As detailed in Table 2, the *Strategic* EI area scores and the *Understanding Emotions* branch scores were found to correlate positively with the activated cluster within the vmPFC.

Additionally, we examined the correlation between MSCEIT scores and the primary condition contrasts. Whereas MSCEIT scores were unrelated to responses to the *Increasing Trustworthiness > Neutral* and *Decreasing Trustworthiness > Neutral* contrasts, MSCEIT scores were found to correlate positively with activation within the emotional regulation region of rostral ACC during the *Decreasing* versus *Increasing Trustworthiness* contrast (see Figure 3b). This cluster was located directly rostral to the genu of the corpus callosum in the right hemisphere [$x = 14$, $y = 44$, $z = 12$], $t(37) = 4.05$, $p = .07$ (FDR small volume corrected), with a cluster extent of 25 voxels. No other regions within the search territories were associated with MSCEIT scores. There were no significant correlations associated with the reverse contrast (i.e., *Increasing Trustworthiness* versus *Decreasing Trustworthiness*). Again, the beta parameters were extracted from the activated cluster region and correlated with MSCEIT subscale scores. This analysis

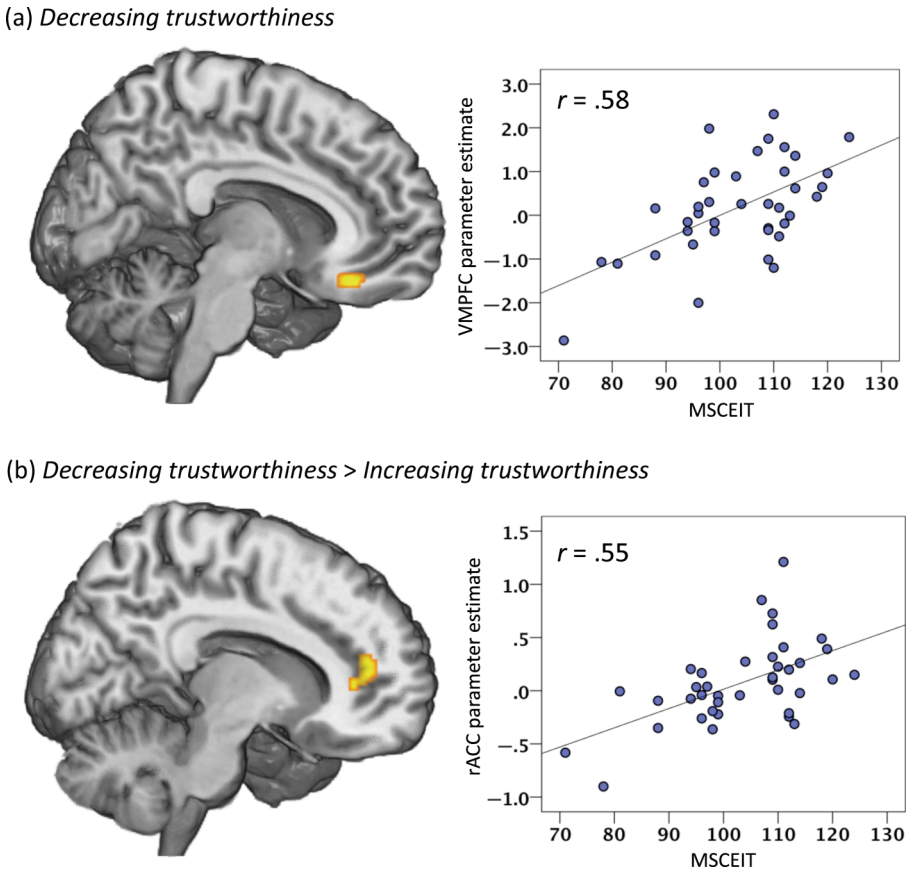


Figure 3. Sagittal brain slices showing significant clusters of activation that correlated with EI, $p < .10$ (small volume corrected), $k \geq 10$. (a) Total scores on the MSCEIT were positively correlated with responses of the ventromedial prefrontal cortex (vmPFC) for the contrast of *Decreasing Trustworthiness* versus implicit baseline (left) [$x = 6$, $y = 32$, $z = -16$]. For visualization purposes, the scatterplot (right) shows the relationship between MSCEIT scores and the first eigenvariate extracted for the entire correlated cluster. (b) Total EI scores on the MSCEIT were positively correlated with responses within the rostral ACC (rACC) for the contrast of *Decreasing* versus *Increasing Trustworthiness* (left) [$x = 14$, $y = 44$, $z = 12$]. For visualization purposes, the scatterplot (right) shows the relationship between MSCEIT scores and the first eigenvariate extracted for the entire correlated cluster.

showed that the rostral ACC cluster was significantly correlated with the two area scores of *Experiential* and *Strategic* EI (see Table 2).

Nonlinear responses

Because of the important role of the amygdala in social and emotional processing of facial expressions and recent evidence suggesting that the amygdala might show a nonlinear pattern of responses to facial trustworthiness (Said, Baron, & Todorov, 2009), we undertook a *post-hoc* analysis to examine potential nonlinear responses of the hypothesized neurocircuitry in the present sample. A test for quadratic trend in the data was evaluated across the three conditions of *Increasing Trustworthiness*, *Neutral*, and *Decreasing Trustworthiness*. Table 3 presents the results of the test for quadratic trend. As evident in Figure 4, significant quadratic trend was found for responses within the right amygdala, vmPFC, and right insular cortex, suggesting significantly greater responses within these regions to images showing either *Increasing* or *Decreasing Trustworthiness* relative to *Neutral* images.

DISCUSSION

The ability to detect dynamic changes in facial cues signifying the intentions of others is vital to human survival. Consistent with prior work (Winston et al., 2002), we found that changes in facial cues reflecting trustworthiness were associated with increased responsiveness of key regions of the SMC, including the vmPFC, amygdala, and insula. We also found that in comparison to a condition of no change in facial

TABLE 2
Correlations between emotional intelligence subscales and cluster activation within the vmPFC and rostral ACC

			fMRI cluster correlation	
Emotional intelligence scale		*Mean (SD)*	*vmPFC [6, 32, –16]*	*rostral ACC [14, 44, 12]*
EQ-i total		103.36 (14.06)		
	Interpersonal	101.44 (15.76)	.317	.158
	Intrapersonal	104.26 (15.66)	.166	.217
	Stress Management	103.31 (12.41)	.168	.138
	Adaptability	102.18 (12.63)	.075	.261
	General mood	104.05 (12.11)	.352	.161
MSCEIT total		103.23 (11.82)		
	Experiential	105.92 (14.75)	.364	.448*
	Perceiving	105.56 (13.89)	.183	.341
	Facilitating	104.44 (14.39)	.426	.414
	Strategic	99.18 (9.67)	.595*	.451*
	Understanding	100.69 (11.89)	.600*	.390
	Managing	97.18 (8.28)	.413	.420

Note: $^{*}p < .005$

TABLE 3
Locations of maximally activated voxels during analysis of quadratic trend across increasing, neutral, and decreasing trustworthiness conditions

		MNI coordinates			
Region	*Cluster size (voxels)*	*x*	*y*	*z*	*SPM {t}*
R insula	27	46	−4	−6	4.41
R insula	66	36	−10	18	3.86
Gyrus rectus	30	0	30	−16	3.65
R amygdala	19	24	0	−16	3.44

Notes: All analyses significant at $p < .001$, uncorrected; $p < .10$ (FDR, small volume corrected). R, right; L, left.

trustworthiness, the activation of these SMC regions was increased regardless of whether the changes in facial attributes involved decreasing or increasing levels of trustworthiness. Given the importance of social trustworthiness judgments to human survival, we further hypothesized that this capacity might be directly related to the construct of EI, a complementary form of intelligence that has been posited to depend critically on the underlying neural system of the SMC (Bar-On et al., 2003). We found that higher scores on one of two standardized and widely used measures of EI were associated with increased activation of specific nodes of the SMC in response to facial feature changes indicative of decreasing trustworthiness during fMRI. Whereas scores on the EQ-i, a self-report *Trait* measure of EI, were unrelated to responsiveness of the SMC to changing trustworthiness, better performance on the MSCEIT, an *Ability* measure of EI, was associated with increased responsiveness of the vmPFC and rostral ACC to these same dynamic changes in facial cues signifying untrustworthiness. Other regions comprising the SMC were not significantly correlated with either index of EI during this task. These findings provide support for the hypothesized role of some components of the SMC in EI, while emphasizing in particular the role of discrete regions of the medial prefrontal cortex and ACC in these capacities.

The SMH posits a central role of the vmPFC in integrating somatic emotional signals with ongoing cognition to guide decision-making (Damasio, 1994, 1996). Indeed, Bar-On and colleagues have suggested that the vmPFC is a critical node of the SMC involved in EI (Bar-On et al., 2003). Presently, we found that the responsiveness of the vmPFC to dynamic facial cues indicating decreasing trustworthiness was positively correlated with MSCEIT *Total EI*, *Strategic EI*, and the *Understanding Emotions* scale. Our finding that individuals with higher MSCEIT scores showed greater responsiveness of the vmPFC to these subtle facial displays indicative of potential threat or dubious character is consistent with a large body of neuroscience evidence pointing to the role of that region in emotional appraisal and emotion regulation. For instance, the process of making inferences about the intentions and emotional states of others, a capacity known as Theory of Mind (ToM), is correlated with increased gray matter volume (Lewis, Rezaie, Brown, Roberts, & Dunbar, 2011) and increased functional activation within the vmPFC (Sebastian et al., 2012). Dysfunction of the vmPFC, whether through actual brain lesions (Leopold et al., 2012) or via disruption of ongoing activity by slow repetitive transcranial magnetic stimulation (rTMS) (Lev-Ran, Shamay-Tsoory, Zangen, & Levkovitz, 2012), also impairs affective ToM performance. Similarly, some evidence suggests that processing of the vmPFC can be disrupted by naturally occurring stresses such as sleep deprivation (Thomas et al., 2000), a process that has been shown to impair emotionally guided moral judgments (Killgore, Killgore, et al., 2007), risky decisions (Killgore, Balkin, & Wesensten, 2006), and *Trait* EI (Killgore, Kahn-Greene, et al., 2007).

Interestingly, we found that the vmPFC responded to changes in facial characteristics indicating either decreasing or increasing trustworthiness. Decreasing

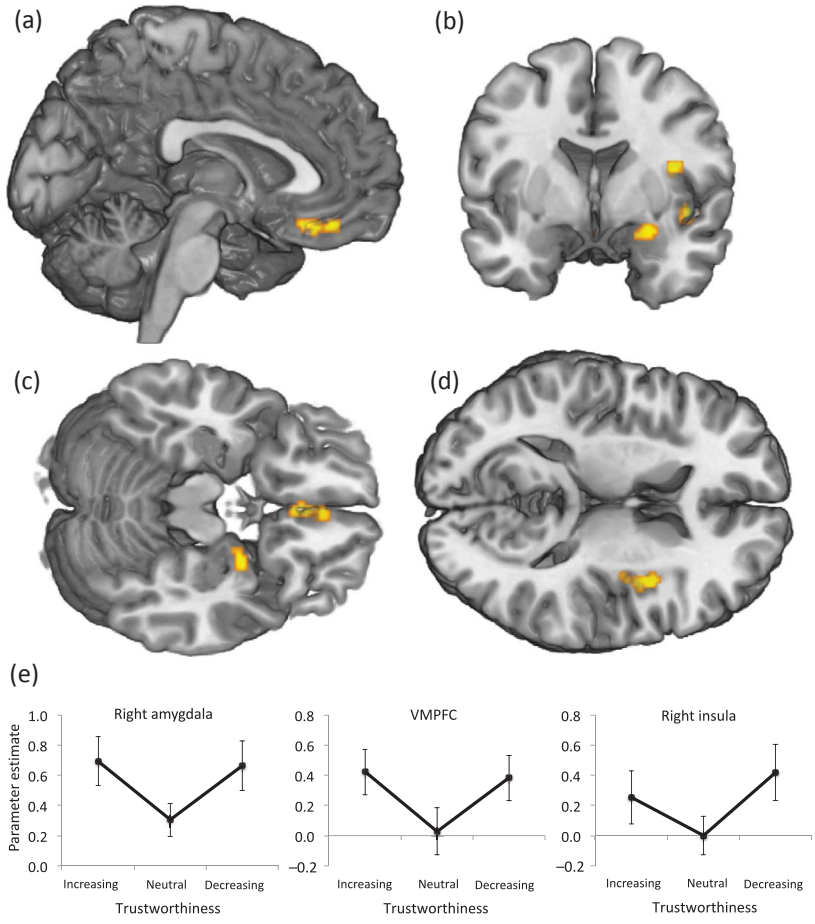


Figure 4. A trend analysis revealed a quadratic pattern of responsiveness across the three trustworthiness conditions of *Increasing Trustworthiness*, *Neutral*, and *Decreasing Trustworthiness* within key regions of interest, including the ventromedial prefrontal cortex (vmPFC), right amygdala, and right insula. Clusters showing this quadratic pattern can be seen on the (a) sagittal slice (vmPFC), (b) coronal slice (right amygdala and insula), slices showing (c) inferior axial (vmPFC and right amygdala), and (d) superior axial (right insula) perspectives. (e) Parameter estimates from the right amygdala, vmPFC, and right insula were extracted from the displayed clusters and plotted for visualization.

trustworthiness was associated with increased activation of a cluster within the gyrus rectus that was centered only about 8 mm anterior to the cluster associated with viewing faces showing increasing trustworthiness. Furthermore, *post-hoc* analyses revealed that a cluster encompassing this same region showed a quadratic pattern of activation, responding to changes in trustworthiness in either direction. Some evidence suggests that the vmPFC represents the reward value of stimuli and plays a role in learning when reinforcement contingencies have changed (Blair, 2008). Kringelbach and Rolls propose that the primary role of the medial orbitofrontal cortex is to represent the reward value of stimuli and to identify when stimuli are no longer reinforcing (Kringelbach & Rolls, 2004), which corresponds well with our findings that this medial prefrontal region was activated when the target faces changed in level of trustworthiness, regardless of whether that change was increasing or decreasing. The vmPFC is also associated with emotional control, including voluntary regulation of negative affect and the corresponding dampening of amygdala responses (Urry et al., 2006). Importantly, the vmPFC has been shown to play a role in the maintenance of extinction memory following fear conditioning in humans (Milad et al., 2007), leading to inhibition of fear responses when encountering a previously feared stimulus (Milad & Quirk, 2002). A recent meta-analysis of neuroimaging studies also showed that patients with posttraumatic stress disorder (PTSD) show abnormal deactivations of the vmPFC (Etkin & Wager, 2007). These findings suggest that the vmPFC may be a key component of resilience and the ability to sustain mental and emotional health following exposure to traumatic events. Our results suggest that this same resilience system is engaged to a greater extent during facial trustworthiness assessments among individuals

showing higher *Ability* EI, as measured by the MSCEIT.

In addition to the vmPFC, a second key region of the SMC, the amygdala, was also activated by dynamic facial cues related to trustworthiness. Direct contrasts between each dynamic trustworthiness condition versus the neutral condition revealed left amygdala activation to *Increasing Trustworthiness* and right amygdala activation to *Decreasing Trustworthiness*. This is consistent with prior research showing that the process of evaluating facial trustworthiness activates the amygdala (Engell, Haxby, & Todorov, 2007; Rule, Krendl, Ivcevic, & Ambady, 2013; Winston et al., 2002), and with a large literature suggesting that the amygdala is involved in detecting facial cues associated with threat and fear (Killgore & Yurgelun-Todd, 2004, 2005; Phelps et al., 2001; Whalen et al., 1998), as well as other emotional expressions (Fitzgerald, Angstadt, Jelsone, Nathan, & Phan, 2006). Furthermore, such responsiveness of the amygdala to trustworthiness information appears to be more strongly correlated with facial features that are commonly agreed upon by consensus raters as a signal of untrustworthiness than to idiosyncratic judgments unique to the individual perceiver (Engell et al., 2007; Rule et al., 2013). Here, we used a standardized set of facial identities that varied on structural facial features that had been previously shown to covary with consensus ratings of trustworthiness (Oosterhof & Todorov, 2008), so we are reasonably confident that the amygdala responses we observed are associated with the differing levels of trustworthiness of the faces. However, it is important to consider that there may be other factors that may contribute to how the facial stimuli were interpreted. Although all of the computer-generated face stimuli used in the present study were designed to display a "neutral" emotional expression, there is some evidence to suggest that structural facial features that resemble emotional expressions can actually affect trait judgments in a systematic manner (Said, Sebe, & Todorov, 2009). For example, Said and colleagues (2009) compared human trait ratings of neutral faces to a computerized face classification system to identify features in the same faces that resembled particular emotions. They found that neutral faces tended to be rated as more positive if they had structural features that resembled expressions of happiness, while features that resembled expressions of anger tended to be judged as more threatening (Said, Sebe, et al., 2009). This tendency to overgeneralize emotions to neutral expressions based solely on the structural features of the face has been shown to affect complex impression formation (Adams, Nelson, Soto, Hess, & Kleck, 2012) and could have contributed to the current findings by giving the visual impression of changing emotion rather than changing trustworthiness per se. Additional research that disentangles these components will be necessary to provide further clarification.

The present findings also need to be considered in light of recent findings suggesting that amygdala responses to facial trustworthiness may not follow a linear pattern (Said, Baron, et al., 2009). Notably, Said, Baron, and Todorov (2009) demonstrated that amygdala responses to facial trustworthiness cues showed a quadratic rather than linear trend, with greater responsiveness to faces judged to be at the extremes of perceived trustworthiness (i.e., either high or low) (Said, Baron, et al., 2009), a finding that has since been replicated (Mattavelli, Andrews, Asghar, Towler, & Young, 2012). Accordingly, we conducted a *post-hoc* analysis of our data to test for nonlinear responses. Our analysis also showed this quadratic pattern for the amygdala, as well as for other SMC regions such as the vmPFC and insula when perceiving facial movement communicating information about potential trustworthiness. Overall, changes in trustworthiness in either direction led to increased activation within specific regions of the SMC, including the amygdala, vmPFC, and insula. In fact, there was no significant difference in the responsiveness of SMC regions when the *Increasing* and *Decreasing Trustworthiness* conditions were directly contrasted, suggesting similar levels of activation.

Although the hypothesized regions showed similar levels of increased activation to both trustworthiness conditions, it was also of interest to examine whether the differential response to decreasing versus increasing trustworthiness of faces might be associated with EI. We found that MSCEIT scores were positively correlated with differential activation of the rostral ACC to displays of decreasing versus increasing trustworthiness. This is important, as the rostral ACC is a brain region that is strongly implicated in error detection (Bush, Luu, & Posner, 2000; Taylor et al., 2006), emotional control (di Pellegrino, Ciaramelli, & Ladavas, 2007), assessing affective salience (Klumpp et al., 2011), and resolving emotional conflict (Etkin et al., 2006). Activation of the rostral ACC is associated with enhanced processing of threatening faces when attentional resources are limited (De Martino, Kalisch, Rees, & Dolan, 2009). Abnormal responses within the rostral ACC have also been reported in a number of psychopathological conditions involving emotional dysregulation such as depression (Cooney, Joormann, Eugene, Dennis, & Gotlib, 2010), posttraumatic stress disorder (Hopper, Frewen, van der Kolk, & Lanius, 2007; Kim et al., 2008), and high trait anxiety (Klumpp et al., 2011). There is evidence to suggest

that the rostral ACC is functionally connected with the amygdala, and that increased rostral ACC activation is frequently associated with corresponding reduction of amygdala responses (Etkin et al., 2006). In our study, we used a task that assesses brain responses to dynamic changes in facial trustworthiness, a social signal that could have important survival implications. This change in the target expression from one of high trustworthiness to one of lesser trustworthiness would be expected to require a rapid reassessment of the intention of the target face, leading to engagement of error detection and affective conflict monitoring regions of the rostral ACC once an initial face assessment was determined to be incorrect. Our finding that increasing rostral ACC activation to these cues correlated with higher scores on the MSCEIT is consistent with the putative role of this region in assessing affective salience, resolving affective conflict, and preparing the individual for a potential response. These findings suggest that individuals with higher *Ability* EI, including both the *Experiential* and *Strategic* aspects, are more sensitive and responsive to these subtle facial cues within this key affective regulating region, potentially conferring a survival advantage.

When considered together, the present findings suggest that greater *Ability* EI is associated with increased responsiveness of the vmPFC region to dynamic facial cues that could communicate the need for increased concern, vigilance, and a potential behavioral response. Higher scores on *Ability* EI and, in particular, subscales assessing the capacity to perceive, respond to, and control emotions (*Experiential* EI), and the ability to understand and direct emotions (*Strategic* EI) were associated with increased responsiveness of the rostral ACC. Because of the role of the rostral ACC in error detection and affective conflict monitoring (Etkin et al., 2006), these findings suggest that greater EI is associated with enhanced responsiveness of these error detection and response systems. However, while the present findings provide partial support to the hypothesized network of the SMC in EI as suggested by Bar-On et al. (2003), there were several regions of this system that failed to show correlated responses with either the EQ-i or MSCEIT. Specifically, although changes in facial trustworthiness were reliably associated with amygdala responses, this activation pattern did not correlate significantly with EI. This was unexpected, but could be related to the nonlinear nature of the amygdala responses, limited power to detect such relationships, or some other indeterminate aspect of our stimuli or experimental design. We did find, however, that *Ability* EI was reliably associated with activation within the medial prefrontal cortex and rostral ACC, suggesting that these emotion regulating and integrating regions appear to play an important role in these capacities. Further work will also be necessary to determine the behavioral implications of these findings, such as whether activation of these EI correlated regions actually confers performance advantages on other emotionally relevant tasks or is related to resilience under actual stressful circumstances. On the other hand, *Trait* EI was not significantly correlated with measured responses within the SMC during the trustworthiness conditions.

CONCLUSION

Greater EI was associated with increased responsiveness of the medial prefrontal cortex during a socially relevant dynamic face perception task, providing partial support for the role of the SMC in these capacities. Discrete nodes of the SMC, including the vmPFC and rostral ACC, were specifically correlated with *Ability* EI capacities, while *Trait* EI was not significantly related to the responsiveness of the hypothesized regions during dynamic facial displays communicating trustworthiness information. Overall, systematic differences in EI capacities appear to be significantly related to the responsiveness of higher order emotion assessment and regulation regions of the medial prefrontal cortex and rostral anterior cingulate.

Original manuscript received 21 November 2012
Revised manuscript accepted 16 May 2013
First published online 26 June 2013

REFERENCES

Adams, R. B. Jr., Nelson, A. J., Soto, J. A., Hess, U., & Kleck, R. E. (2012). Emotion in the neutral face: A mechanism for impression formation? *Cognition & Emotion*, *26*(3), 431–441.

Adolphs, R., Tranel, D., & Damasio, A. R. (1998). The human amygdala in social judgment. *Nature*, *393*(6684), 470–474.

Bar-On, R. (2002). *BarOn emotional quotient inventory: A measure of emotional intelligence—Technical manual*. North Tonawanda, NY: Multi-Health Systems.

Bar-On, R. (2006). The Bar-On model of emotional-social intelligence (ESI). *Psicothema*, *18*(*Suppl*), 13–25.

Bar-On, R., Tranel, D., Denburg, N. L., & Bechara, A. (2003). Exploring the neurological substrate of emotional and social intelligence. *Brain*, *126*(Pt 8), 1790–1800.

Bechara, A., & Damasio, A. (2005). The somatic marker hypothesis: A neural theory of economic decision. *Games and Economic Behavior*, *52*, 336–372.

Blair, R. J. (2008). The amygdala and ventromedial prefrontal cortex: Functional contributions and dysfunction in psychopathy. *Philosophical Transactions of the Royal*

Society of London. Series B, Biological Sciences, *363*(1503), 2557–2565.

Brackett, M. A., & Mayer, J. D. (2003). Convergent, discriminant, and incremental validity of competing measures of emotional intelligence. *Personality & Social Psychology Bulletin*, *29*(9), 1147–1158.

Bush, G., Luu, P., & Posner, M. I. (2000). Cognitive and emotional influences in anterior cingulate cortex. *Trends in Cognitive Sciences*, *4*(6), 215–222.

Bzdok, D., Langner, R., Hoffstaedter, F., Turetsky, B. I., Zilles, K., & Eickhoff, S. B. (2012). The modular neuroarchitecture of social judgments on faces. *Cerebral Cortex*, *22*(4), 951–961.

Cooney, R. E., Joormann, J., Eugene, F., Dennis, E. L., & Gotlib, I. H. (2010). Neural correlates of rumination in depression. *Cognitive, Affective & Behavioral Neuroscience*, *10*(4), 470–478.

Damasio, A. R. (1994). *Descartes' error: Emotion, reason and the human brain*. New York, NY: Grosset/Putnam.

Damasio, A. R. (1996). The somatic marker hypothesis and the possible functions of the prefrontal cortex. *Philosophical Transactions of the Royal Society B: Biological Sciences*, *351*(1346), 1413–1420.

De Martino, B., Kalisch, R., Rees, G., & Dolan, R. J. (2009). Enhanced processing of threat stimuli under limited attentional resources. *Cerebral Cortex*, *19*(1), 127–133.

di Pellegrino, G., Ciaramelli, E., & Ladavas, E. (2007). The regulation of cognitive control following rostral anterior cingulate cortex lesion in humans. *Journal of Cognitive Neuroscience*, *19*(2), 275–286.

Engell, A. D., Haxby, J. V., & Todorov, A. (2007). Implicit trustworthiness decisions: Automatic coding of face properties in the human amygdala. *Journal of Cognitive Neuroscience*, *19*(9), 1508–1519.

Etkin, A., Egner, T., & Kalisch, R. (2011). Emotional processing in anterior cingulate and medial prefrontal cortex. *Trends in Cognitive Sciences*, *15*(2), 85–93.

Etkin, A., Egner, T., Peraza, D. M., Kandel, E. R., & Hirsch, J. (2006). Resolving emotional conflict: A role for the rostral anterior cingulate cortex in modulating activity in the amygdala. *Neuron*, *51*(6), 871–882.

Etkin, A., & Wager, T. D. (2007). Functional neuroimaging of anxiety: A meta-analysis of emotional processing in PTSD, social anxiety disorder, and specific phobia. *American Journal of Psychiatry*, *164*(10), 1476–1488.

First, M. B., Spitzer, R. L., Gibbon, M., & Williams, J. B. W. (2002). *Structured clinical interview for DSM-IV-TR Axis I Disorders, research version, patient edition. (SCID-I/P)*. New York, NY: Biometrics Research Department, New York State Psychiatric Institute.

Fitzgerald, D. A., Angstadt, M., Jelsone, L. M., Nathan, P. J., & Phan, K. L. (2006). Beyond threat: Amygdala reactivity across multiple expressions of facial affect. *Neuroimage*, *30*(4), 1441–1448.

Frith, C. D. (2007). The social brain? *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*, *362*(1480), 671–678.

Gardner, H. (1983). *Frames of mind: The theory of multiple intelligences*. New York, NY: Basic Books.

Goleman, D. (1995). *Emotional intelligence*. New York, NY: Bantam.

Hopper, J. W., Frewen, P. A., van der Kolk, B. A., & Lanius, R. A. (2007). Neural correlates of reexperiencing, avoidance, and dissociation in PTSD: Symptom dimensions and emotion dysregulation in responses to script-driven trauma imagery. *Journal of Traumatic Stress*, *20*(5), 713–725.

Killgore, W. D., Weber, M., Schwab, Z. J., Deldonno, S. R., Kipman, M., Weiner, M. R., & Rauch, S. L. (2012). Gray matter correlates of Trait and Ability models of emotional intelligence. *Neuroreport*, *23*(9), 551–555.

Killgore, W. D. S., Balkin, T. J., & Wesensten, N. J. (2006). Impaired decision-making following 49 hours of sleep deprivation. *Journal of Sleep Research*, *15*, 7–13.

Killgore, W. D. S., Kahn-Greene, E. T., Lipizzi, E. L., Newman, R. A., Kamimori, G. H., & Balkin, T. J. (2007). Sleep deprivation reduces perceived emotional intelligence and constructive thinking skills. *Sleep Medicine*, *9*, 517–526.

Killgore, W. D. S., Killgore, D. B., Day, L. M., Li, C., Kamimori, G. H., & Balkin, T. J. (2007). The effects of 53 hours of sleep deprivation on moral judgment. *Sleep*, *30*(3), 345–352.

Killgore, W. D. S., & Yurgelun-Todd, D. A. (2004). Sex-related developmental differences in the lateralized activation of the prefrontal cortex and amygdala during perception of facial affect. *Perceptual and Motor Skills*, *99*(2), 371–391.

Killgore, W. D. S., & Yurgelun-Todd, D. A. (2005). Social anxiety predicts amygdala activation in adolescents viewing fearful faces. *Neuroreport*, *16*(15), 1671–1675.

Killgore, W. D. S., & Yurgelun-Todd, D. A. (2007). Neural correlates of emotional intelligence in adolescent children. *Cognitive, Affective, and Behavioral Neuroscience*, *7*(2), 140–151.

Kim, M. J., Chey, J., Chung, A., Bae, S., Khang, H., Ham, B., . . . Lyoo, I. K. (2008). Diminished rostral anterior cingulate activity in response to threat-related events in posttraumatic stress disorder. *Journal of Psychiatric Research*, *42*(4), 268–277.

Klumpp, H., Ho, S. S., Taylor, S. F., Phan, K. L., Abelson, J. L., & Liberzon, I. (2011). Trait anxiety modulates anterior cingulate activation to threat interference. *Depression and Anxiety*, *28*(3), 194–201.

Koscik, T. R., & Tranel, D. (2011). The human amygdala is necessary for developing and expressing normal interpersonal trust. *Neuropsychologia*, *49*(4), 602–611.

Koven, N. S., Roth, R. M., Garlinghouse, M. A., Flashman, L. A., & Saykin, A. J. (2011). Regional gray matter correlates of perceived emotional intelligence. *Social Cognitive and Affective Neuroscience*, *6*(5), 582–590.

Kreifelts, B., Ethofer, T., Huberle, E., Grodd, W., & Wildgruber, D. (2010). Association of trait emotional intelligence and individual fMRI-activation patterns during the perception of social signals from voice and face. *Human Brain Mapping*, *31*(7), 979–991.

Kringelbach, M. L., & Rolls, E. T. (2004). The functional neuroanatomy of the human orbitofrontal cortex: Evidence from neuroimaging and neuropsychology. *Progress in Neurobiology*, *72*(5), 341–372.

Leopold, A., Krueger, F., Dal Monte, O., Pardini, M., Pulaski, S. J., Solomon, J., & Grafman, J. (2012). Damage to the left ventromedial prefrontal cortex impacts affective theory of mind. *Social Cognitive and Affective Neuroscience*, *7*(8), 871–880.

Lev-Ran, S., Shamay-Tsoory, S. G., Zangen, A., & Levkovitz, Y. (2012). Transcranial magnetic stimulation of the ventromedial prefrontal cortex impairs theory of

mind learning. *European Psychiatry: The Journal of the Association of European Psychiatrists*, *27*(4), 285–289.

Lewis, P. A., Rezaie, R., Brown, R., Roberts, N., & Dunbar, R. I. (2011). Ventromedial prefrontal volume predicts understanding of others and social network size. *NeuroImage*, *57*(4), 1624–1629.

Maldjian, J. A., Laurienti, P. J., Kraft, R. A., & Burdette, J. H. (2003). An automated method for neuroanatomic and cytoarchitectonic atlas-based interrogation of fMRI data sets. *Neuroimage*, *19*(3), 1233–1239.

Mattavelli, G., Andrews, T. J., Asghar, A. U., Towler, J. R., & Young, A. W. (2012). Response of face-selective brain regions to trustworthiness and gender of faces. *Neuropsychologia*, *50*(9), 2205–2211.

Mayer, J. D., Salovey, P., & Caruso, D. R. (2002). *Mayer-Salovey-Caruso Emotional Intelligence Test (MSCEIT) User's manual*. North Tonawanda, NY: MHS.

Mayer, J. D., Salovey, P., Caruso, D. R., & Sitarenios, G. (2001). Emotional intelligence as a standard intelligence. *Emotion*, *1*(3), 232–242.

Milad, M. R., & Quirk, G. J. (2002). Neurons in medial prefrontal cortex signal memory for fear extinction. *Nature*, *420*(6911), 70–74.

Milad, M. R., Wright, C. I., Orr, S. P., Pitman, R. K., Quirk, G. J., & Rauch, S. L. (2007). Recall of fear extinction in humans activates the ventromedial prefrontal cortex and hippocampus in concert. *Biology Psychiatry*, *62*(5), 446–454.

Oosterhof, N. N., & Todorov, A. (2008). The functional basis of face evaluation. *Proceedings of the National Academy of Sciences of the United States of America*, *105*(32), 11087–11092.

Phelps, E. A., O'Connor, K. J., Gatenby, J. C., Gore, J. C., Grillon, C., & Davis, M. (2001). Activation of the left amygdala to a cognitive representation of fear. *Nature Neuroscience*, *4*(4), 437–441.

Reis, D. L., Brackett, M. A., Shamosh, N. A., Kiehl, K. A., Salovey, P., & Gray, J. R. (2007). Emotional Intelligence predicts individual differences in social exchange reasoning. *Neuroimage*, *35*(3), 1385–1391.

Rule, N. O., Krendl, A. C., Ivcevic, Z., & Ambady, N. (2013). Accuracy and consensus in judgments of trustworthiness from faces: Behavioral and neural correlates. *Journal of Personality and Social Psychology*, *104*(3), 409–426.

Said, C. P., Baron, S. G., & Todorov, A. (2009). Nonlinear amygdala response to face trustworthiness: Contributions of high and low spatial frequency information. *Journal of Cognitive Neuroscience*, *21*(3), 519–528.

Said, C. P., Sebe, N., & Todorov, A. (2009). Structural resemblance to emotional expressions predicts evaluation of emotionally neutral faces. *Emotion*, *9*(2), 260–264.

Sebastian, C. L., Fontaine, N. M., Bird, G., Blakemore, S. J., Brito, S. A., McCrory, E. J., & Viding, E. (2012). Neural processing associated with cognitive and affective theory of mind in adolescents and adults. *Social Cognitive and Affective Neuroscience*, *7*(1), 53–63.

Takeuchi, H., Taki, Y., Sassa, Y., Hashizume, H., Sekiguchi, A., Fukushima, A., & Kawashima, R. (2011). Regional gray matter density associated with emotional intelligence: Evidence from voxel-based morphometry. *Human Brain Mapping*, *32*(9), 1497–1510.

Taylor, S. F., Martis, B., Fitzgerald, K. D., Welsh, R. C., Abelson, J. L., Liberzon, I., . . . Gehring, W. J. (2006). Medial frontal cortex activity and loss-related responses to errors. *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience*, *26*(15), 4063–4070.

Thomas, M., Sing, H., Belenky, G., Holcomb, H., Mayberg, H., Dannals, R., . . . Redmond, D. (2000). Neural basis of alertness and cognitive performance impairments during sleepiness. I. Effects of 24 h of sleep deprivation on waking human regional brain activity. *Journal of Sleep Research*, *9*(4), 335–352.

Tzourio-Mazoyer, N., Landeau, B., Papathanassiou, D., Crivello, F., Etard, O., Delcroix, N., . . . Joliot, M. (2002). Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. *Neuroimage*, *15*(1), 273–289.

Urry, H. L., van Reekum, C. M., Johnstone, T., Kalin, N. H., Thurow, M. E., Schaefer, H. S., . . .Davidson, R. J. (2006). Amygdala and ventromedial prefrontal cortex are inversely coupled during regulation of negative affect and predict the diurnal pattern of cortisol secretion among older adults. *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience*, *26*(16), 4415–4425.

Webb, C. A., Schwab, Z. J., Weber, M., DelDonno, S., Kipman, M., Weiner, M. R., & Killgore, W. D. S. (2013). Convergent and divergent validity of integrative versus mixed model measures of emotional intelligence. *Intelligence*, *41*(3), 149–156.

Wechsler, D. (1958). *The measurement and appraisal of adult intelligence* (4th ed.). Baltimore, MD: Williams & Wilkins.

Whalen, P. J., Rauch, S. L., Etcoff, N. L., McInerney, S. C., Lee, M. B., & Jenike, M. A. (1998). Masked presentations of emotional facial expressions modulate amygdala activity without explicit knowledge. *Journal of Neuroscience*, *18*(1), 411–418.

Winston, J. S., Strange, B. A., O'Doherty, J.., & Dolan, R. J. (2002). Automatic and intentional brain responses during evaluation of trustworthiness of faces. *Nature Neuroscience*, *5*(3), 277–283.

Physical exercise and brain responses to images of high-calorie food

William D.S. Killgore[a,b], Maia Kipman[a], Zachary J. Schwab[a], Olga Tkachenko[a], Lily Preer[a], Hannah Gogel[a], John S. Bark[a], Elizabeth A. Mundy[a,b], Elizabeth A. Olson[a,b] and Mareen Weber[a,b]

Physical exercise has many health benefits, including improved cardiovascular fitness, lean muscle development, increased metabolism, and weight loss, as well as positive effects on brain functioning and cognition. Recent evidence suggests that regular physical exercise may also affect the responsiveness of reward regions of the brain to food stimuli. We examined whether the total number of minutes of self-reported weekly physical exercise was related to the responsiveness of appetite and food reward-related brain regions to visual presentations of high-calorie and low-calorie food images during functional MRI. Second, we examined whether such responses would correlate with self-reported food preferences. While undergoing scanning, 37 healthy adults (22 men) viewed images of high-calorie and low-calorie foods and provided desirability ratings for each food image. The correlation between exercise minutes per week and brain responses to the primary condition contrast (high-calorie > low-calorie) was evaluated within the amygdala, insula, and medial orbitofrontal cortex, brain regions previously implicated in responses to food images. Higher levels of exercise were significantly correlated with lower responsiveness within the medial orbitofrontal cortex and left insula to high-calorie foods. Furthermore, activation of these regions was positively correlated with preference ratings for high-calorie foods, particularly those with a savory flavor. These findings suggest that physical exercise may be associated with reduced activation in food-responsive reward regions, which are in turn associated with reduced preferences for unhealthy high-calorie foods. Physical exercise may confer secondary health benefits beyond its primary effects on cardiovascular fitness and energy expenditure. *NeuroReport* **00:000–000 © 2013 Wolters Kluwer Health | Lippincott Williams & Wilkins.**

NeuroReport 2013, **00**:000–000

Keywords: calorie, food, functional magnetic resonance imaging, insula, orbitofrontal cortex, physical exercise

[a]Center for Depression, Anxiety, and Stress Research, McLean Hospital, Belmont and [b]Department of Psychiatry, Harvard Medical School, Boston, Massachusetts, USA

Correspondence to William D.S. Killgore, PhD, Center for Depression, Anxiety, and Stress Research, McLean Hospital, Harvard Medical School, 115 Mill Street, Belmont, MA 02478, USA
Tel: +617 855 3166; fax: +617 855 2770; e-mail: killgore@mclean.harvard.edu

Received 18 June 2013 **accepted** 20 August 2013

Introduction

Physical exercise has numerous beneficial effects on health, including improved cardiovascular fitness, lean muscle development, increased metabolism, and weight loss, among others [1]. Recent evidence suggests that regular physical activity may also affect food consumption, which could further contribute to the health benefits of exercise. The effects of physical exercise on appetite and food intake are complex and not fully understood, but empirical evidence suggests that while greater physical activity may increase fasting hunger sensations, it may also lead to improvements in the satiety response and control over aspects of appetite regulation [2]. One potential mechanism for greater appetite control may be alterations in the subjective reward value of food. Recent functional neuroimaging findings suggest that chronic regular exercise may be associated with reduced responsiveness of brain reward regions, such as the insula and cingulate gyrus, to visual food cues in overweight individuals [3,4]. While some reward regions seem to show reduced responsiveness to food images after a chronic exercise program, it is not clear whether these brain activation changes directly relate to reduced desire to consume the food represented in the images.

Using functional MRI, we examined the association between self-reported weekly physical exercise levels and brain responses to images of food differing in calorie density. We surveyed several key regions associated with appetite regulation and the assessment of reward value for visually presented food stimuli, specifically the amygdala, insula, and medial orbitofrontal cortex (mOFC) [5–7]. We hypothesized that individuals with higher levels of physical exercise per week would show reduced responsiveness of these key regions when viewing images of high-calorie versus low-calorie foods, and that the activation of these regions would correlate positively with self-rated desirability of high-calorie food items.

Methods

Participants

Thirty-seven healthy adults (15 women; 22 men) between 18–45 years (mean = 29.7; SD = 8.4) of age completed questionnaires about exercise habits and

0959-4965 © 2013 Wolters Kluwer Health | Lippincott Williams & Wilkins DOI: 10.1097/WNR.0000000000000029

underwent functional neuroimaging. Exclusionary criteria included any significant history of medical, neurological, or psychiatric problems, illicit substance use, alcohol treatment, recent use of psychoactive medications, and abnormal visual acuity not correctable with contact lenses. Although the present findings are novel and have never been published previously, other data from a subset of this same sample have been reported elsewhere [8,9]. Participants ranged from normal weight to moderately obese, with an average BMI of 24.5 (SD = 3.7; range 19.8–34.8). Written informed consent was provided before enrollment and all participants were compensated for their time. This research protocol was reviewed and approved by the Institutional Review Board of McLean Hospital.

Materials and procedure

Exercise questionnaire

Following informed consent, each participant completed several self-report questionnaires about food intake on the day of the scan, as well as typical dietary, sleep, and exercise habits. In particular, participants answered questions about their typical physical exercise routines, including the number of exercise sessions completed during an average week and the typical duration of their workouts. The product of these two values was calculated to derive each individual's typical exercise minutes per week. Participants consumed an average of 323.5 calories (SD = 245.5; range 0–929.5) throughout the day before undergoing the scan, but had no food intake for an hour before entering the scanner.

Neuroimaging

While undergoing functional MRI, participants viewed a series of food and nonfood images presented in 30-s blocks that alternated between pictures of foods differing in calorie density, including high-calorie (H) foods (e.g. cheeseburgers, ice cream, cake, French fries, candy), low-calorie (L) foods (e.g. fresh salads, vegetables, fruits, fresh fish, whole grain bread), or control (C) images (i.e. nonedible rocks, flowers, shrubs). The paradigm is similar to that reported in our previous publications [5,10,11]. Briefly, food and control stimuli were presented in seven alternating stimulus blocks of 10 images each (3 s/image), bounded at the beginning and end by a 15-s fixation cross (+) presented in the following order (+ , C, L, H, C, H, L, C, +). The entire scan lasted 240 s. Following the scan, the participants completed an offline rating for each of the food images, indicating on a seven-point scale how much they desired to eat the depicted food item at that moment. For analysis, the food images were further subdivided into those with flavors that were either savory (e.g. cheeseburgers, green salads; H = 9; L = 12) or sweet (e.g., ice cream, fruit; H = 11; L = 8).

Magnetic resonance imaging parameters

Scans were collected using a 3.0-T Siemens Tim Trio scanner (Siemens, Erlangen, Germany) and a 12-channel head coil. First, structural T1-weighted 3D MPRAGE images were collected for anatomical coregistration (TR/TE/flip angle = 2.1 s/2.25 ms/12°) over 128 sagittal slices (256 × 256 matrix) providing a slice thickness of 1.33 mm (voxel size = 1 × 1 × 1.33 mm). For functional scanning, we collected a T2*-weighted echo planar imaging sequence (TR/TE/flip angle = 3.0 s/30 ms/90°) with 80 images/slice over 43 transverse interleaved planes (3.5 mm thickness, no skip; 22.4 cm field of view; 64 × 64 acquisition matrix), yielding a voxel size of 3.5 × 3.5 × 3.5 mm. To ensure steady-state equilibrium, the first three functional scans were discarded before data collection.

Image processing

Data were preprocessed and analyzed in SPM8 (Wellcome Department of Cognitive Neurology, London, UK), using standard realignment and motion correction parameters. The echo planar imaging images were coregistered, spatially normalized, and smoothed using an isotropic Gaussian kernel (full width at half maximum = 6 mm), and resliced to 2 × 2 × 2 mm. Time series data were convolved with the canonical hemodynamic response function and the effects of serial autocorrelation were removed with a first-level autoregressive model. The default 128-s high-pass filter was used to remove low-frequency drift in the signal.

Statistical analysis

Within SPM8, a series of general linear models were created for the H, L, and C conditions against an implicit baseline, followed by construction of a direct contrast between the high-calorie versus low-calorie conditions. In a second-level random effects regression model, these contrast images were correlated with the previously calculated variable of interest, exercise minutes per week. Because previous work has suggested that men and women process images of food stimuli differently [11], participant sex was entered as a nuisance covariate. According to our *a priori* hypotheses, the primary analyses were restricted to six search territories (i.e. bilateral insula, amygdala, and mOFC) as defined by the Automated Anatomical Labeling Atlas [12], implemented within the Wake Forest University SPM8 Toolbox PickAtlas Utility (*http://www.fmri.wfubmc.edu/downloads/WFU_PickAtlas_User_Manual.pdf*) [13]. Statistical thresholds were selected with consideration to the guidelines for principled correction for false positives [14]. Accordingly, activation maps for the regression analyses were initially thresholded at P less than 0.001 uncorrected, k (extent) at least 10 contiguous voxels (based on the expected number of voxels per cluster as reported in the SPM output, which was $k = 11.1$; this was rounded down to $k \geq 10$ for consistency with other publications), and then subjected to small volume correction for multiple comparisons within each search territory at P less than 0.05, corrected for false discovery rate. Significant clusters within the search territories were extracted and

correlated in SPSS 20 (IBM Corporation, Armonk, New York, USA) with postscan food desirability ratings made by the participants for each of the food images.

Results

Physical exercise

Twenty-five participants (67.6%) reported engaging in regular physical exercise (i.e. at least once a week or more), whereas 12 (32.4%) indicated that they did not exercise with any regularity, or at all. The number of reported workout days per week for the entire sample ranged from 0 to 7 (mean = 2.8, SD = 2.3). The average duration of workouts ranged from 0 to 120 min (mean = 38.4, SD = 36.1). For each individual, the product of these variables was calculated as the average number of exercise minutes per week, which ranged from 0 to 540 min (mean = 151.1, SD = 159.9).

Neuroimaging

Voxel-wise correlation analysis was used to examine the association between exercise minutes per week and responses within each of the search territories for the H > L contrast. As shown in Fig. 1a, exercise minutes per week was significantly negatively correlated with a cluster of 10 voxels within the mOFC (MNI coordinates: $x = 0$, $y = 48$, $z = -10$; $T[34] = 3.58$; $R^2 = 0.28$). Similarly, Fig. 1b shows that exercise minutes per week was negatively correlated with a cluster of *22* voxels in the left anterior insula (MNI coordinates: $x = -30$, $y = 128$, $z = 160$; $T[34] = 4.32$; $R^2 = 0.35$). In contrast, there were no clusters in the right or left amygdala where exercise minutes per week was significantly correlated with responses to the H > L contrast. Furthermore, there were no clusters in any regions showing positive correlations with exercise minutes per week.

Correlations with food ratings

The first eigenvariate was extracted from significant clusters in the preceding analysis and correlated with each individual's exercise minutes per week and food ratings. As shown in Table 1, exercise minutes per week was negatively correlated with preference ratings for savory high-calorie foods. In addition, extracted data from the mOFC and left insula (in response to the H > L contrast) were positively correlated with preference ratings for savory high-calorie foods, but not for sweet high-calorie foods. None of these variables were related to ratings for low-calorie foods.

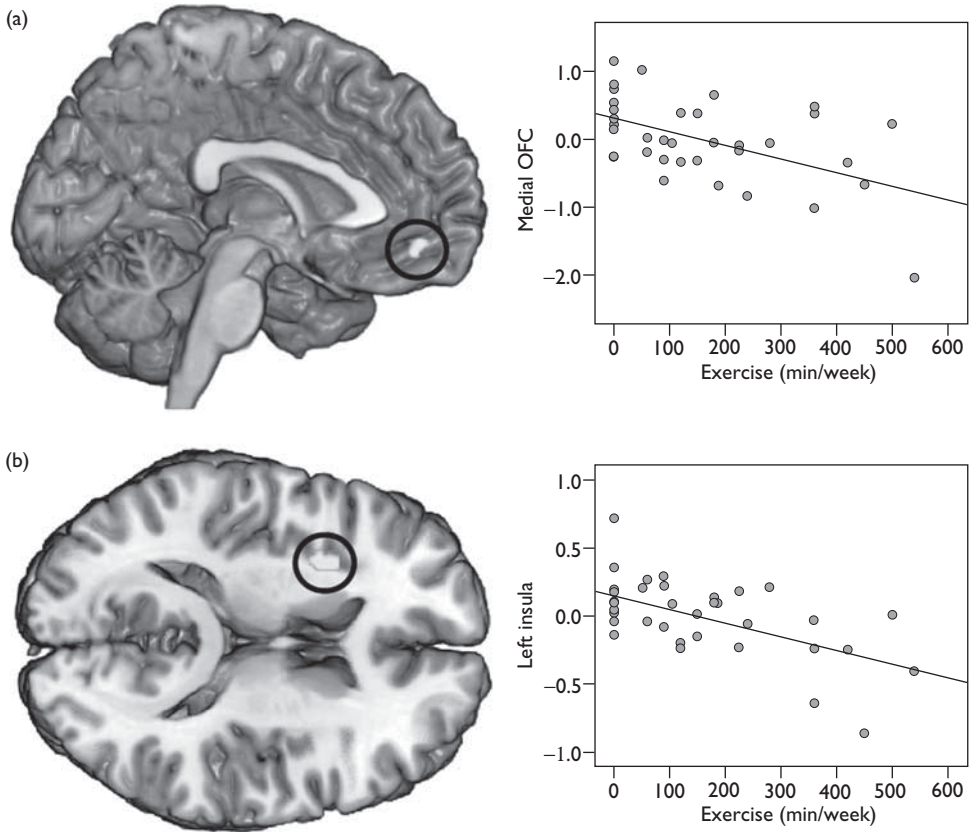
Discussion

We examined the association between self-reported physical exercise minutes and brain responses to visually presented images of high-calorie versus low-calorie-dense foods. Greater physical exercise was significantly correlated with reduced activation within the mOFC and left anterior insula in response to foods with higher calorie density. The insula plays a major role in visceral interoceptive sensations and has been associated with craving for drugs and food [15]. The mOFC also appears to be a key region in processing the reward value of stimuli, particularly pleasure responses to preferred foods [16]. Furthermore, we also found that the magnitude of these brain responses was positively associated with self-rated desire to consume the specific high-calorie foods presented, particularly those foods with a savory flavor (e.g. cheeseburgers, French fries, hot dogs), whereas those with a sweet flavor (e.g. ice cream, cake, chocolate candy) did not show a significant association. In short, regular physical exercise was associated with reduced responsiveness of appetite-related brain regions, and this lower responsiveness was associated with reduced preference and desire for high-calorie foods.

These findings build upon an emerging literature that suggests that physical exercise may contribute to weight loss in ways that extend beyond simple energy expenditure and altered metabolism. Research evidence indicates that exercise may also alter brain responses to food stimuli, particularly within reward processing and appetite-related regions such as the orbitofrontal cortex and insula. For instance, in a recent study, researchers found that a 60-min bout of acute exercise led to an immediate postworkout reduction in the responsiveness of the orbitofrontal cortex, insula, and other reward-related brain regions during presentation of high-calorie foods [17]. Findings from that study are consistent with evidence suggesting that acute exercise not only burns calories, but also leads to reduced food intake. This likely occurs due to alterations in brain systems involved in pleasure responses and salience processing, leading to reduced incentive motivation toward food [3,18]. Moreover, the effects on brain functioning do not appear to be limited to acute postexercise changes, as insular responses to high-calorie food images were attenuated following a 6-month exercise program [3,4] and were highly correlated with actual weight loss and body fat reduction [3]. Such findings suggest that the effects of exercise on brain functioning are sustained and not simply a transient effect of acute physical activity. Our data are congruent with these previous findings, suggesting that even self-reported habitual exercise levels are reliably associated with reduced insula and mOFC responses to images of high-calorie foods. Moreover, our findings extend previous work by showing that reduced activation within these brain regions was also associated with reduced desire to consume high-calorie foods, particularly those with a savory flavor. This could be particularly important for weight reduction, as preference for savory foods has been posited as a risk factor for overweight and obesity [19].

The exact mechanisms by which exercise may exert the observed effects on brain functioning remain to be determined, but recent studies suggest that exercise may lead to an enhancement of leptin sensitivity in animals [20]

Fig. 1



Self-reported physical exercise (minutes per week) was negatively correlated with responses within the (a) medial orbitofrontal cortex (OFC) (MNI: $x=0$, $y=48$, $z=-10$) and (b) left insula (MNI: $x=-30$, $y=128$, $z=160$) superimposed on the standard T1 template from SPM8. Scatterplots are displayed for descriptive purposes and show the pattern of association between exercise and the first extracted cluster eigenvariate. MNI, Montreal Neurological Institute.

Table 1 Mean food ratings and Pearson correlations with exercise minutes per week and extracted brain activation clusters

Food rating	Mean (SD)	Exercise (min/week)	mOFC (0, 48, −10)	L insula (−30, 12, 16)
High calorie	4.3 (1.2)	−0.14	0.32†	0.36*
Savory	4.3 (1.5)	−0.33*	0.33*	0.33*
Sweet	4.3 (1.5)	0.06	0.20	0.25
Low calorie	3.7 (1.4)	0.06	0.00	0.10
Savory	3.5 (1.4)	0.06	−0.02	0.14
Sweet	4.0 (1.5)	0.05	0.04	0.03

Coordinates are within stereotaxic space of the Montreal Neurological Institute.
L, left; mOFC, medial orbitofrontal cortex.
*$P<0.05$.
†$P<0.10$.

and humans [21]. As leptin can affect insula and prefrontal cortex responses to food stimuli [22], it is possible that the effects of exercise on leptin sensitivity may be one avenue for this effect. It is also conceivable that cardiovascular fitness alters basic brain physiology and information processing, leading to greater neural efficiency. Exercise is associated with many beneficial effects on brain structure and function, including neuroplastic changes [23], increased blood flow [24] and neurogenesis within the hippocampus [25], as well as the proliferation of new blood vessels within the brain [26]. However, the specificity of the effects we observed to high-calorie versus low-calorie foods argues against a simple improvement in global brain functioning, suggesting instead that greater physical activity was associated with specific and circumscribed responses of appetite and food relevant regions such as the insula and orbitofrontal cortex. The data are, of course, correlational

and could be affected by other factors. One alternate explanation would be that the observed correlations are due to the influence of an unmeasured third variable, such as heightened health awareness or fitness consciousness, which may drive the frequency of exercise as well as the decreased preference for calorie-dense foods. Further research into the potential causes of these specific changes will be an important step toward understanding the association between physical activity and brain function.

In contrast to the findings for the mOFC and insula, we did not find any significant correlation between physical exercise and amygdala responses. Our previous work has shown that the amygdala is responsive to both high-calorie and low-calorie food images [5] and that this pattern of activation appears to be developmentally invariant between childhood and early adulthood [10]. This invariance of activation suggests that the amygdala response to food is established early in development and may reflect a broad and generic salience response to the presence of food irrespective of calorie density or hedonic value. The present findings further suggest that the responsiveness of the amygdala to food images remains relatively stable irrespective of chronic levels of physical exercise.

While the present results suggest that there is a significant association between regular physical exercise and reduced responses to high-calorie food stimuli within specific appetite and reward processing regions of the brain, the findings should be interpreted in light of some limitations. First, our findings are based on subjective estimates of exercise frequency and duration per week, which may be less reliable than objective measures such as wrist actigraphy or heart rate monitoring. Second, we did not specify the type of exercise in which participants engaged (e.g. cardiovascular training, strength training), which could potentially have differential effects on brain functioning or appetite. This would be an important area for further study. Third, to permit some variability in brain responses to food, we did not specifically restrict dietary intake during the day of the scan, although no food was allowed for an hour before neuroimaging. This could have added further variance in the data, and future work should consider controlling food intake on the day of scanning. Fourth, our method used statistical control for false positives as implemented in SPM8, which may influence the probability of type I versus type II errors. Alternate approaches for correction, such as Monte Carlo simulations might also be appropriate for consideration in future analyses. Finally, the present data are correlational, so the causal direction of the association cannot be inferred. Further research will be necessary to determine whether there is a causal link between exercise, brain responsiveness, and food desire, or whether all may be driven by general attitudes surrounding health and fitness consciousness. Nevertheless, the present findings are intriguing and suggest that there are significant associations between physical exercise and the responsiveness of key appetite and reward regions related to food intake.

Conclusion

Self-reported regular physical exercise was associated with reduced functional responses to calorie-rich foods within brain regions involved in reward processing, appetite, and visceral interoceptive sensations, including the mOFC and insula. Moreover, lower activation in clusters in these regions was significantly correlated with reduced preference ratings for specific high-calorie foods, particularly those with a savory flavor. While it is well established that physical exercise increases calorie expenditure and cardiovascular fitness, our findings raise the possibility that regular physical exercise may also have indirect effects on health by diminishing functional brain activation in regions that influence preferences for less-healthy high-calorie foods.

Acknowledgements

This study was supported by a USAMRAA grant (W81XWH-09-1-0730) to WDSK.

Conflicts of interest

There are no conflicts of interest.

References

1 O'Gorman DJ, Krook A. Exercise and the treatment of diabetes and obesity. *Endocrinol Metab Clin North Am* 2008; **37**:887–903.

2 Martins C, Kulseng B, King NA, Holst JJ, Blundell JE. The effects of exercise-induced weight loss on appetite-related peptides and motivation to eat. *J Clin Endocrinol Metab* 2010; **95**:1609–1616.

3 Cornier MA, Melanson EL, Salzberg AK, Bechtell JL, Tregellas JR. The effects of exercise on the neuronal response to food cues. *Physiol Behav* 2012; **105**:1028–1034.

4 Nock NL, Dimitropolous A, Tkach J, Frasure H, von Gruenigen V. Reduction in neural activation to high-calorie food cues in obese endometrial cancer survivors after a behavioral lifestyle intervention: a pilot study. *BMC Neurosci* 2012; **13**:74.

5 Killgore WDS, Young AD, Femia LA, Bogorodzki P, Rogowska J, Yurgelun-Todd DA. Cortical and limbic activation during viewing of high- versus low-calorie foods. *Neuroimage* 2003; **19**:1381–1394.

6 Killgore WDS, Yurgelun-Todd DA. Body mass predicts orbitofrontal activity during visual presentations of high-calorie foods. *Neuroreport* 2005; **16**:859–863.

7 Killgore WDS, Yurgelun-Todd DA. Affect modulates appetite-related brain activity to images of food. *Int J Eat Disord* 2006; **39**:357–363.

8 Killgore WD, Schwab ZJ. Sex differences in the association between physical exercise and IQ. *Percept Mot Skills* 2012; **115**:605–617.

9 Killgore WD, Schwab ZJ, Weber M, Kipman M, Deldonno SR, Weiner MR, *et al.* Daytime sleepiness affects prefrontal regulation of food intake. *Neuroimage* 2013; **71**:216–223.

10 Killgore WDS, Yurgelun-Todd DA. Developmental changes in the functional brain responses of adolescents to images of high and low-calorie foods. *Dev Psychobiol* 2005; **47**:377–397.

11 Killgore WDS, Yurgelun-Todd DA. Sex differences in cerebral responses to images of high versus low-calorie food. *Neuroreport* 2010; **21**:354–358.

12 Tzourio-Mazoyer N, Landeau B, Papathanassiou D, Crivello F, Etard O, Delcroix N, *et al.* Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. *Neuroimage* 2002; **15**:273–289.

13 Maldjian JA, Laurienti PJ, Kraft RA, Burdette JH. An automated method for neuroanatomic and cytoarchitectonic atlas-based interrogation of fMRI data sets. *Neuroimage* 2003; **19**:1233–1239.
14 Bennett CM, Wolford GL, Miller MB. The principled control of false positives in neuroimaging. *Soc Cogn Affect Neurosci* 2009; **4**:417–422.
15 Tang DW, Fellows LK, Small DM, Dagher A. Food and drug cues activate similar brain regions: a meta-analysis of functional MRI studies. *Physiol Behav* 2012; **106**:317–324.
16 Small DM, Zatorre RJ, Dagher A, Evans AC, Jones-Gotman M. Changes in brain activity related to eating chocolate: from pleasure to aversion. *Brain* 2001; **124**:1720–1733.
17 Evero N, Hackett LC, Clark RD, Phelan S, Hagobian TA. Aerobic exercise reduces neuronal responses in food reward brain regions. *J Appl Physiol* 2012; **112**:1612–1619.
18 Hagobian TA, Yamashiro M, Hinkel-Lipsker J, Streder K, Evero N, Hackney T. Effects of acute exercise on appetite hormones and ad libitum energy intake in men and women. *Appl Physiol Nutr Metab* 2013; **38**:66–72.
19 Maffeis C, Grezzani A, Perrone L, Del Giudice EM, Saggese G, Tato L. Could the savory taste of snacks be a further risk factor for overweight in children? *J Pediatr Gastroenterol Nutr* 2008; **46**:429–437.
20 Kang S, Kim KB, Shin KO. Exercise training improves leptin sensitivity in peripheral tissue of obese rats. *Biochem Biophys Res Commun* 2013; **435**:454–459.
21 Jones TE, Basilio JL, Brophy PM, McCammon MR, Hickner RC. Long-term exercise training in overweight adolescents improves plasma peptide YY and resistin. *Obesity (Silver Spring)* 2009; **17**:1189–1195.
22 Baicy K, London ED, Monterosso J, Wong ML, Delibasi T, Sharma A, *et al*. Leptin replacement alters brain response to food cues in genetically leptin-deficient adults. *Proc Natl Acad Sci U S A* 2007; **104**:18276–18279.
23 Van Praag H. Exercise and the brain: something to chew on. *Trends Neurosci* 2009; **32**:283–290.
24 Pereira AC, Huddleston DE, Brickman AM, Sosunov AA, Hen R, McKhann GM, *et al*. An in vivo correlate of exercise-induced neurogenesis in the adult dentate gyrus. *Proc Natl Acad Sci U S A* 2007; **104**:5638–5643.
25 Van Praag H, Kempermann G, Gage FH. Running increases cell proliferation and neurogenesis in the adult mouse dentate gyrus. *Nat Neurosci* 1999; **2**:266–270.
26 Voss MW, Nagamatsu LS, Liu-Ambrose T, Kramer AF. Exercise, brain, and cognition across the life span. *J Appl Physiol* 2011; **111**:1505–1513.